1. I need a search on the compounds of formula I below, (with the R groups taken into account shown in claim 1):

I

Docket No.: 0233i0.53093US

What is claimed is:

1. A substituted 4-aminocyclohexanol compound corresponding to formula I,

I

wherein

R^1 and R^2 independently of one another represent H; C_{1-8}-alkyl or C_{3-8}-cycloalkyl, in each case saturated or unsaturated, branched or unbranched, mono- or polysubstituted or unsubstituted; aryl- or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or aryl, C_{3-8}-cycloalkyl or heteroaryl bonded via C_{1-4}-alkylene and in each case mono- or polysubstituted or unsubstituted; wherein R^1 and R^2 are not both H, or

the radicals R^1 and R^2 together form a ring and represent $CH_2CH_2OCH_2CH_2$, $CH_2CH_2NR^6CH_2CH_2$ or $(CH_2)_{3-6}$,

wherein

R^6 represents H; C_{1-8}-alkyl or C_{3-8}-cycloalkyl, in each case saturated or unsaturated, branched or unbranched, mono- or polysubstituted or unsubstituted; aryl- or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or aryl, C_{3-8}-cycloalkyl or heteroaryl bonded via C_{1-4}-alkylene and in each case mono- or polysubstituted or unsubstituted;

Docket No.: 029310-5103US

R^5 represents C_{1-8}-alkyl or C_{3-8}-cycloalkyl, in each case saturated or unsaturated, branched or unbranched, mono- or polysubstituted or unsubstituted, or aryl, C_{3-8}-cycloalkyl or heteroaryl bonded via a saturated or unsaturated, branched or unbranched, substituted or unsubstituted C_{1-4}-alkyl group and in each case unsubstituted or mono- or polysubstituted;

R^6 represents C_{3-8}-cycloalkyl, aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted, $-CHR^8R^9$, $-CHR^8-CH_2R^9$, $-CHR^8-CH_2-CH_2R^9$, $-CHR^8-CH_2-CHOR^9$, $-C(Y)R^9$, $-C(Y)-CH_2R^9$, $-C(Y)-CH_2-CH_2R^9$ or $-C(Y)-CH_2-CH_2-CH_2R^9$; or $-R^8$-L-R^9

wherein

Y = O, S or H_2;

R^8 represents H; C_{1-6}-alkyl, saturated or unsaturated, branched or unbranched, mono- or polysubstituted or unsubstituted; or $C(O)O$-C_{1-6}-alkyl, saturated or unsaturated, branched or unbranched, mono- or polysubstituted or unsubstituted;

R^9 represents H; C_{3-8}-cycloalkyl, aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted;

R^8 represents aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted;

L represents -C(O)-NH-, -NH-C(O)-, -C(O)-O-, -O-C(O)-, -O-, -S- or $-S(O)_2$-; and

R^9 represents aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted,

or a salt thereof with a physiologically tolerated acid.


```
=> fil cap
FILE 'CAPLUS' ENTERED AT 12:06:56 ON 28 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 28 Mar 2008 VOL 148 ISS 14
FILE LAST UPDATED: 27 Mar 2008 (20080327/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

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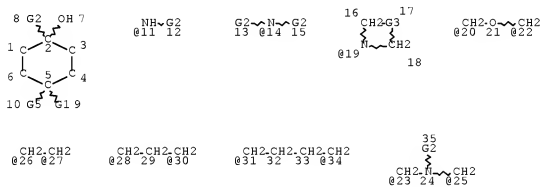
L2 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
L4 190 SEA FILE=REGISTRY SSS FUL L2
L5 19 SEA FILE=CAPLUS ABB=ON PLU=ON L4

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L5 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:94964 CAPLUS Full-text
DOCUMENT NUMBER: 148:191845
TITLE: Preparation of cyclohexylindoles as opioid receptor-like 1 (ORL1) receptor inhibitors
INVENTOR(S): Zemolka, Saskia; Schunk, Stefan; Englberger, Werner; Koegel, Babette-Yvonne; Linz, Klaus; Schick, Hans; Sonnenschein, Helmut; Graubaum, Heinz; Hinze, Claudia
PATENT ASSIGNEE(S): Gruenenthal GmbH, Germany
SOURCE: PCT Int. Appl., 303pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008009415	A2	20080124	WO 2007-EP6325	20070717
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
DE 102006033109	A1	20080131	DE 2006-102006033109	20060718
PRIORITY APPLN. INFO.:			DE 2006-102006033109A	20060718
OTHER SOURCE(S):			MARPAT 148:191845	

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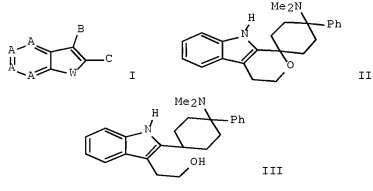
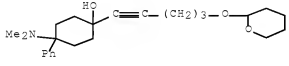


AB Title compds. I [A = N, CR7-10; B, C = H, alkyl, cycloalkyl, etc.; R7, R8, R9, R10 = H, halo, NO2, etc.; W = O, S, NR4, preferably NH; R4 = H, C1-5 alkyl,

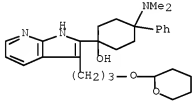
etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, tin-mediated reduction of pyranose II gave the citrate salt of claimed indole III. In ORL1 receptor inhibition assays, 6 examples of compds. I exhibited Ki values ranging from 0.0009-3 μM.

IT 1004545-33-8P 1004547-27-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of cyclohexylindoles as opioid receptor-like 1 (ORL1) receptor inhibitors)

RN 1004545-33-8 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-phenyl-1-[5-[(tetrahydro-2H-pyran-2-yl)oxy]-1-pentyn-1-yl]- (CA INDEX NAME)

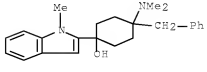


RN 1004547-27-6 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-phenyl-1-[3-[3-[(tetrahydro-2H-pyran-2-yl)oxy]propyl]-1H-pyrrolo[2,3-b]pyridin-2-yl]- (CA INDEX NAME)



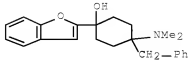
IT 492462-14-3P 492462-23-4P 1004548-14-4P
1004548-15-5P 1004548-20-2P 1004548-21-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclohexylindoles as opioid receptor-like 1 (ORL1) receptor inhibitors)

RN 492462-14-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(1-methyl-1H-indol-2-yl)-4-(phenylmethyl)- (CA INDEX NAME)

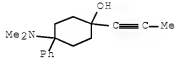


RN 492462-23-4 CAPLUS

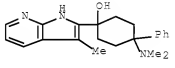
CN Cyclohexanol, 1-(2-benzofuranyl)-4-(dimethylamino)-4-(phenylmethyl)- (CA INDEX NAME)



RN 1004548-14-4 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-phenyl-1-(1-propyn-1-yl)- (CA INDEX NAME)

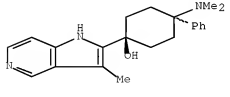


RN 1004548-15-5 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(3-methyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-4-phenyl- (CA INDEX NAME)



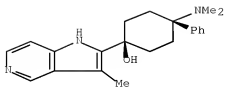
RN 1004548-20-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(3-methyl-1H-pyrrolo[3,2-c]pyridin-2-yl)-4-phenyl-, cis- (CA INDEX NAME)

Relative stereochemistry.



RN 1004548-21-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(3-methyl-1H-pyrrolo[3,2-c]pyridin-2-yl)-4-phenyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1021606 CAPLUS Full-text
DOCUMENT NUMBER: 143:326096
TITLE: Preparation of substituted urea and carbamate, phenacyl-2-hydroxy-3-diaminoalkane, and benzamide-2-hydroxy-3-diaminoalkane aspartyl protease and β-secretase inhibitors for treating conditions associated with amyloidosis such as Alzheimer's disease
INVENTOR(S): John, Varghese; Maillard, Michel; Tucker, John; Aquino, Jose; Hom, Roy; Tung, Jay; Dressen, Darren; Shah, Neerav; Neitz, R. Jeffrey
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 532 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087215	A1	20050922	WO 2005-US7775	20050309
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2558249	A1	20050922	CA 2005-2558249	20050309
US 2005261273	A1	20051124	US 2005-75292	20050309
EP 1734942	A1	20061227	EP 2005-725123	20050309
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007528404	T	20071011	JP 2007-502963	20050309

PRIORITY APPLN. INFO.:

US 2004-551192P	P	20040309
US 2004-575829P	P	20040602
US 2004-591857P	P	20040729
US 2004-622589P	P	20041028
WO 2005-US7775	W	20050309

OTHER SOURCE(S): MARPAT 143:326096

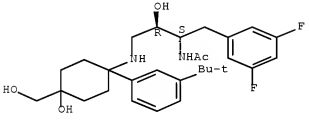
AB The invention is related to compds. of formula R2NHCH(R1)CH(OH)CH2NHRc (I) [R1 = (un)substituted benzyl, thien-2-ylmethyl, etc.; R2 = NH2 and derivs., SO2-aryl, hetero/aryl-U, etc.; U = CO, CS, CONH and derivs., etc.; Rc = carbocyclyl or heterocyclyl; with addnl. details given in the claims] particularly acetyl 2-hydroxy-1,3-diaminospirocyclohexanes and derivs., that are useful in treating diseases, disorders, and conditions associated with amyloidosis. Amyloidosis refers to a collection of diseases, disorders, and conditions associated with abnormal deposition of A-β protein. For example, alkylation of (2R,3S)-3-amino-1-[[1-(3-tert- butylphenyl)cyclohexyl]amino]-4-(3,5-difluorophenyl)butan-2-ol•2HCl with 4-iodobenzamide gave the coresponding amide. Selected I displayed IC50 values < 5 μM in a cell free inhibition assay utilizing a synthetic APP substrate that can be cleaved by β-secretase. The selectivity of I for β-secretase vs. cathepsin D for 6 examples of I are tabulated. Brain uptake, total polar surface area and/or lipophilicity for 32 examples of I are tabulated.

IT 861933-83-7P, N-[(1S,2R)-3-[[1-(3-tert-Butylphenyl)-4-hydroxy-4-hydroxymethylcyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of as aspartyl protease and β-secretase inhibitors)

RN 861933-83-7 CAPLUS

CN Acetamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[1-[3-(1,1-dimethylethyl)phenyl]-4-hydroxy-4-(hydroxymethyl)cyclohexyl]amino]-2-hydroxypropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:696731 CAPLUS Full-text

DOCUMENT NUMBER: 143:193724

TITLE: Preparation of N-(3-amino-2-hydroxypropyl)acetamides as aspartyl protease and beta secretase inhibitors for treating conditions associated with amyloidosis such as Alzheimer's disease

INVENTOR(S): John, Varghese; Hom, Roy; Sealy, Jennifer; Aquino, Jose; Probst, Gary; Tung, Jay; Fang, Larry

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 499 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070407	A1	20050804	WO 2005-US1875	20050121
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2006014790	A1	20060119	US 2005-38790	20050121
EP 1729755	A1	20061213	EP 2005-711743	20050121
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PRIORITY APPLN. INFO.:

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US 2004-537580P	P	20040121
US 2004-575798P	P	20040602
US 2004-575799P	P	20040602
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US 2004-591885P	P	20040729
US 2004-591908P	P	20040729
US 2004-619917P	P	20041020
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WO 2005-US1875	W	20050121

OTHER SOURCE(S): MARPAT 143:193724
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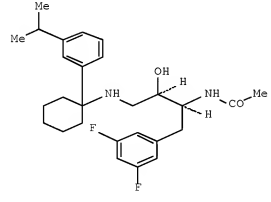


I

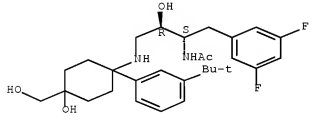
AB The invention relates to N-(3-amino-2-hydroxypropyl)acetamides (R2CH2C(O)NHCHR1CH(OH)CH2NHRc (I); R1 = (un)substituted benzyl, thien-2-ylmethyl, etc.; R2 = H and F; Rc = carbocyclyl or heterocyclyl; addnl. details are given in the claims; e.g. N-[(1S,2R)-1-(3,5- difluorobenzyl)-2-hydroxy-3-[[1-(3-isopropylphenyl)cyclohexyl]amino]propyl]acetamide hydrochloride (free base shown as II)) that are useful in treating diseases, disorders, and conditions associated with amyloidosis. Amyloidosis refers to a collection of diseases, disorders, and conditions associated with abnormal deposition of A-beta protein. Although the methods of preparation are not claimed, .apprx.200 example prepns. of I and intermediates are included. For example, II was prepared in 3 steps (77, unknown and 87% yields) starting from 1-(3-isopropylphenyl)cyclohexanamine hydrochloride and [(1S)-2-(3,5-difluorophenyl)-1-((2S)-oxiran-2- yl)ethyl]carbamic acid tert-Bu ester and involving intermediates tert-Bu [(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[1-(3- isopropylphenyl)cyclohexyl]amino]propyl]carbamate and (2R,3S)-3-amino-4- (3,5-difluorophenyl)-1-[[1-(3-isopropylphenyl)cyclohexyl]amino]butan-2-ol dihydrochloride. Efficacy for 10 examples of I for inhibiting amyloid-beta peptide in the cortex and/or plasma are tabulated. The selectivity of I for β-secretase vs. cathepsin D for 92 examples of I are tabulated. Oral bioavailability for one I was determined in male rats. Brain uptake, total polar surface area and/or lipophilicity for 32 examples of I are tabulated.

IT 861933-83-7P, N-[(1S,2R)-3-[[1-(3-tert-Butylphenyl)-4-hydroxy-4-hydroxymethylcyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of N-(3-amino-2-hydroxypropyl)acetamides as aspartyl protease and beta secretase inhibitors for treating conditions associated with amyloidosis such as Alzheimer's disease)

RN 861933-83-7 CAPLUS

CN Acetamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[1-[3-(1,1-dimethylethyl)phenyl]-4-hydroxy-4-(hydroxymethyl)cyclohexyl]amino]-2-hydroxypropyl]- (CA INDEX NAME)

Absolute stereochemistry.



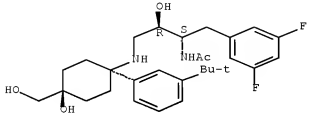
IT 861860-00-6P, N-[(1S,2R)-3-[[cis-1-(3-tert-Butylphenyl)-4-hydroxy-4-hydroxymethylcyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide 861860-01-7P, N-[(1S,2R)-3-[[trans-1-(3-tert-Butylphenyl)-4-hydroxy-4-hydroxymethylcyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide 861860-36-8P, N-[3-[[1-(3-tert-Butylphenyl)-4-hydroxy-4-hydroxymethylcyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-(3-amino-2-hydroxypropyl)acetamides as aspartyl protease and beta secretase inhibitors for treating conditions associated with amyloidosis such as Alzheimer's disease)

RN 861860-00-6 CAPLUS

CN Acetamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[cis-1-[3-(1,1-dimethylethyl)phenyl]-4-hydroxy-4-(hydroxymethyl)cyclohexyl]amino]-2-hydroxypropyl]- (CA INDEX NAME)

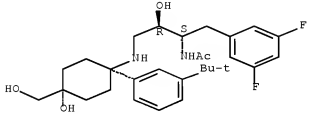
Absolute stereochemistry.



RN 861860-01-7 CAPLUS

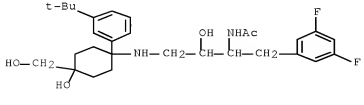
CN Acetamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[trans-1-[3-(1,1-dimethylethyl)phenyl]-4-hydroxy-4-(hydroxymethyl)cyclohexyl]amino]-2-hydroxypropyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 861860-36-8 CAPLUS

CN Acetamide, N-[1-[(3,5-difluorophenyl)methyl]-3-[[1-[3-(1,1-dimethylethyl)phenyl]-4-hydroxy-4-(hydroxymethyl)cyclohexyl]amino]-2-hydroxypropyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:310829 CAPLUS Full-text
DOCUMENT NUMBER: 140:303552
TITLE: Preparation of β-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-α
INVENTOR(S): Duan, Jingwu; King, Bryan W.; Decicco, Carl; Maduskuie, Thomas P.; Voss, Mathew E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 150 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004072802	A1	20040415	US 2002-267207	20021009

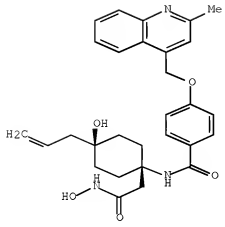
PRIORITY APPLN. INFO.: US 2002-267207 20021009
OTHER SOURCE(S): MARPAT 140:303552

AB Novel β-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 [Ra1 = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ra1 may form a ring], CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRa1)r1O(CRaRa1)r-Q (r, r1 = 0-4), (CRaRa1)r1NRa(CRaRa1)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRa1)r1O(CRaRa1)r-Q1, (CRaRa1)r1NRa(CRaRa1)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepared as metalloprotease and TNF-α inhibitors. Thus, N-hydroxy-1-[[4-[(2- methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepared by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

IT 362701-92-6P 362701-93-7P 362702-25-8P 362702-26-9P 362702-37-2P 362702-38-3P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

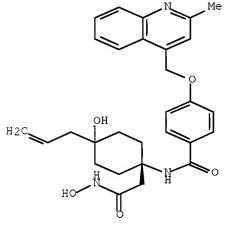
RN 362701-92-6 CAPLUS
CN Benzamide, N-[trans-4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(2-propenyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



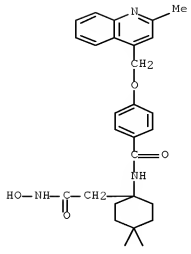
RN 362701-93-7 CAPLUS
CN Benzamide, N-[cis-4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(2-propenyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 362702-25-8 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(methoxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (CA INDEX NAME)

PAGE 1-A



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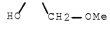
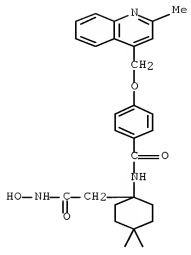


RN 362702-26-9 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(methoxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362702-25-8
CMF C28 H33 N3 O6

PAGE 1-A



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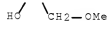
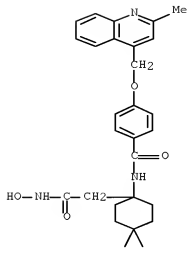


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 362702-37-2 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(hydroxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (CA INDEX NAME)

PAGE 1-A



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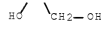

RN 362702-38-3 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(hydroxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

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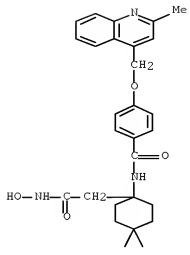
CRN 362702-37-2
CMF C27 H31 N3 O6

PAGE 1-A



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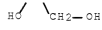


CM 2

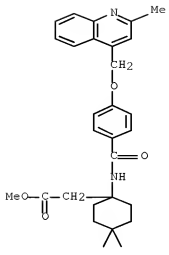
CRN 76-05-1
CMF C2 H F3 O2

IT 362706-44-3P 362706-61-4P 362706-62-5P
362706-67-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

RN 362706-44-3 CAPLUS

CN Cyclohexaneacetic acid, 4-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-4-(2-propenyl)-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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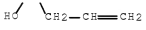
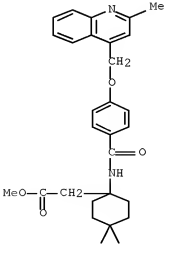


RN 362706-61-4 CAPLUS
CN Cyclohexaneacetic acid, 4-hydroxy-4-(methoxymethyl)-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, methyl ester (CA INDEX NAME)

PAGE 1-A



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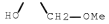
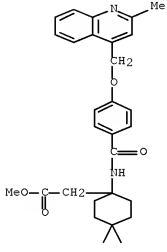


RN 362706-62-5 CAPLUS
CN Cyclohexaneacetic acid, 4-hydroxy-4-(3-hydroxypropyl)-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, methyl ester (CA INDEX NAME)

PAGE 1-A



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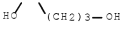
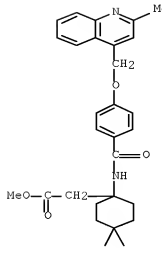


RN 362706-67-0 CAPLUS
CN Cyclohexaneacetic acid, 4-hydroxy-4-(hydroxymethyl)-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, methyl ester (CA INDEX NAME)

PAGE 1-A



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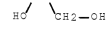


L5 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:341731 CAPLUS Full-text
DOCUMENT NUMBER: 139:332906
TITLE: Opioid activity of C8813, a novel and potent opioid analgesic
AUTHOR(S): Liu, Zhong-Hua; Jin, Wen-Qiao; Dai, Qi-Yuan; Chen, Xin-Jian; Zhang, Hong-Ping; Chi, Zhi-Qiang
CORPORATE SOURCE: Shanghai Institutes for Biological Sciences, Shanghai Institute of Materia Medica, 2nd Department of Pharmacology, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Life Sciences (2003), 73(2), 233-241
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Compound trans-4-(p-bromophenyl)-4-(dimethylamino)-1-(2-thiophen-2-yl-ethyl)-cyclohexanol (C8813), structurally unrelated to morphine, is a novel analgesic. The present study examined the antinociception, opioid receptor selectivity and in vitro activity of C8813. The antinociceptive activity was evaluated using mouse hot plate and acetic acid writhing tests. In mouse hot plate test, the antinociceptive ED50 of C8813 was 11.5 μg/kg, being 591 times and 3.4 times more potent than morphine and fentanyl resp. In mouse writhing test, the antinociceptive ED50 of C8813 was 16.9 μg/kg, being 55 times and 2.3 times more active than morphine and fentanyl resp. In the opioid receptor binding assay, C8813 showed high affinity for μ-opioid receptor (Ki = 1.37 nM)

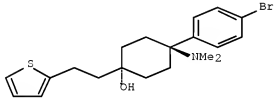
and δ-opioid receptor (Ki = 3.24 nM) but almost no affinity for κ-opioid receptor (at 1 μM). In the bioassay, the inhibitory effect of C8813 in the guinea-pig ileum (GPI) was 16.5 times more potent than in the mouse vas deferens (MVD). The inhibitory effects of C8813 in the GPI and MVD could be antagonized by μ-opioid receptor antagonist naloxone and δ-opioid receptor antagonist ICI174,864 resp. However, the inhibitory effect of C8813 in the rabbit vas deferens was very weak. These results indicated that C8813 was a potent analgesic and a high affinity agonist for the μ- and δ-opioid receptors.

IT 616898-54-5P, C 8813
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(opioid activity of novel analgesic C8813)

RN 616898-54-5 CAPLUS

CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-[2-(2-thienyl)ethyl]-, trans- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:76742 CAPLUS Full-text
DOCUMENT NUMBER: 138:137023
TITLE: Preparation of 4-amino-4-(arylalkyl)cyclohexanols as ORL1 receptor ligands for treatment of pain
INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-heinrich; Koegel, Babette-yvonne; Wnendt, Stephan
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008371	A1	20030130	WO 2002-EP7849	20020715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,				

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10135635	A1	20030206	DE 2001-10135635		20010717
DE 10135637	A1	20030206	DE 2001-10135637		20010717
CA 2453843	A1	20030130	CA 2002-2453843		20020715
AU 2002328894	A1	20030303	AU 2002-328894		20020715
AU 2002328894	B2	20070614			
EP 1406859	A1	20040414	EP 2002-764691		20020715
EP 1406859	B1	20080102			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002011223	A	20040810	BR 2002-11223		20020715
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CN 1555355	A	20041215	CN 2002-817915		20020715
JP 2005504742	T	20050217	JP 2003-513932		20020715
NZ 531112	A	20050930	NZ 2002-531112		20020715
AT 382601	T	20080115	AT 2002-764691		20020715
RU 2315750	C2	20080127	RU 2004-104628		20020715
MX 2004PA00272	A	20040504	MX 2004-PA272		20040109
NO 2004000162	A	20040311	NO 2004-162		20040114
US 2004214822	A1	20041028	US 2004-758241		20040116
ZA 2004001223	A	20041130	ZA 2004-1223		20040216
PRIORITY APPLN. INFO.:			DE 2001-10135635	A	20010717
			DE 2001-10135637	A	20010717
			WO 2002-EP7849	W	20020715

OTHER SOURCE(S): MARPAT 138:137023

GI

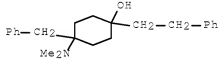
I

AB Title compds. I [wherein R1 and R2 = independently H or (un)substituted (cyclo)alkyl; or NR1R2 = morpholinyl, (un)substituted piperazinyl, pyrrolidinyl, piperidinyl, etc.; R3 = (cyclo)alkyl optionally substituted with cycloalkyl or (hetero)aryl; R4 = (un)substituted cycloalkyl or (hetero)aryl; and racemates, stereoisomers, pharmaceutically acceptable salts, and hydrates thereof] were prepared for treating various indications, especially pain. For example, reaction of 1,4-dioxaspiro[4.5]decan-8-one with dimethylamine•HCl and KCN gave 3-dimethylamino-1,4- dioxaspiro[4.5]decane-8-nitrile. Substitution with benzylmagnesium chloride, conversion to the cyclohexanone, addition of phenethylmagnesium chloride, and recrystn. afforded 4-benzyl-4-dimethylamino-1- phenethylcycloexanol•HCl. The latter exhibited binding to the ORL1 opioid receptor with Ki of 0.02 μM and demonstrated analgesic activity in the mouse tail flick test with ED50 of 0.015 mg/kg i.v.

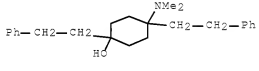
IT 492461-58-2P, 4-Benzyl-4-dimethylamino-1-phenethylcyclohexanol
492461-62-8P, 4-Dimethylamino-1,4-diphenethylcyclohexanol
492461-64-0P, 4-Benzyl-4-dimethylamino-1-[2-(2-fluorophenyl)ethyl]cyclohexanol 492461-66-2P, 4-Benzyl-4-dimethylamino-1-[2-(4-fluorophenyl)ethyl]cyclohexanol

492461-70-8P, 4-Dimethylamino-4-(2-fluorobenzyl)-1-phenethylcyclohexanol 492461-74-2P, 4-Dimethylamino-4-(3-fluorobenzyl)-1-phenethylcyclohexanol 492461-78-6P, 4-Dimethylamino-4-(4-fluorobenzyl)-1-phenethylcyclohexanol 492461-83-3P, 4-Benzyl-4-dimethylamino-1-(2-fluorobenzyl)cyclohexanol 492461-92-4P 492461-96-8P, 4-Benzyl-4-dimethylamino-1-(3-fluorobenzyl)cyclohexanol 492462-01-8P, 4-Benzyl-4-dimethylamino-1-(4-fluorobenzyl)cyclohexanol 492462-12-1P, 4-Benzyl-1-phenethyl-4-(pyrrolidin-1-yl)cyclohexanol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(analgesic; preparation of (amino)(arylalkyl)cyclohexanol analgesics starting from dioxaspiro[4.5]decanones, amines, and arylalkylmagnesium chlorides)

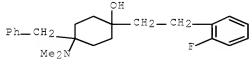
RN 492461-58-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(2-phenylethyl)-4-(phenylmethyl)- (CA INDEX NAME)



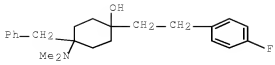
RN 492461-62-8 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1,4-bis(2-phenylethyl)- (CA INDEX NAME)



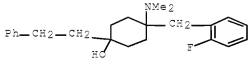
RN 492461-64-0 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(2-fluorophenyl)ethyl]-4-(phenylmethyl)- (CA INDEX NAME)



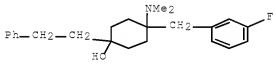
RN 492461-66-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-4-(phenylmethyl)- (CA INDEX NAME)



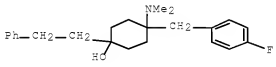
RN 492461-70-8 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(2-fluorophenyl)methyl]-1-(2-phenylethyl)- (CA INDEX NAME)



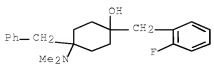
RN 492461-74-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(3-fluorophenyl)methyl]-1-(2-phenylethyl)- (CA INDEX NAME)



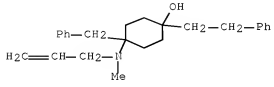
RN 492461-78-6 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(4-fluorophenyl)methyl]-1-(2-phenylethyl)- (CA INDEX NAME)



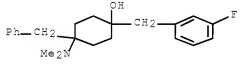
RN 492461-83-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[(2-fluorophenyl)methyl]-4-(phenylmethyl)- (CA INDEX NAME)



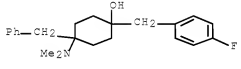
RN 492461-92-4 CAPLUS
CN Cyclohexanol, 4-(methyl-2-propenylamino)-1-(2-phenylethyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



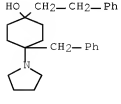
RN 492461-96-8 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[(3-fluorophenyl)methyl]-4-(phenylmethyl)- (CA INDEX NAME)



RN 492462-01-8 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[(4-fluorophenyl)methyl]-4-(phenylmethyl)- (CA INDEX NAME)

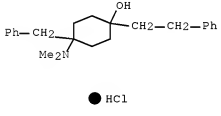


RN 492462-12-1 CAPLUS
CN Cyclohexanol, 1-(2-phenylethyl)-4-(phenylmethyl)-4-(1-pyrrolidinyl)- (CA INDEX NAME)

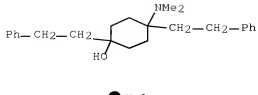


IT 492461-57-1P, 4-Benzyl-4-dimethylamino-1-phenethylcyclohexanol hydrochloride 492461-59-3P, 4-Dimethylamino-1,4-diphenethylcyclohexanol hydrochloride 492461-63-9P, 4-Benzyl-4-dimethylamino-1-[2-(2-fluorophenyl)ethyl]cyclohexanol hydrochloride 492461-65-1P, 4-Benzyl-4-dimethylamino-1-[2-(4-fluorophenyl)ethyl]cyclohexanol hydrochloride 492461-67-3P, 4-Dimethylamino-4-(2-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-71-9P, 4-Dimethylamino-4-(3-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-75-3P, 4-Dimethylamino-4-(4-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-81-1P, 4-Benzyl-4-dimethylamino-1-(2-fluorobenzyl)cyclohexanol hydrochloride 492461-85-5P 492461-94-6P, 4-Benzyl-4-dimethylamino-1-(3-fluorobenzyl)cyclohexanol hydrochloride 492461-98-0P, 4-Benzyl-4-dimethylamino-1-(4-fluorobenzyl)cyclohexanol hydrochloride 492462-03-0P, 1-Benzyl-4-dimethylamino-4-(3-fluorobenzyl)cyclohexanol hydrochloride 492462-05-2P, 4-Benzyl-1-phenethyl-4-(pyrrolidin-1-yl)cyclohexanol hydrochloride 492462-14-3P, 4-Benzyl-4-dimethylamino-1-(1-methyl-1H-indol-2-yl)cyclohexanol 492462-16-5P, 1-Benzo[b]thiophen-2-yl-4-benzyl-4-dimethylaminocyclohexanol 492462-21-2P, 1-Benzo[b]thiophen-3-yl-4-benzyl-4-dimethylaminocyclohexanol 492462-23-4P, 1-Benzofuran-2-yl-4-benzyl-4-dimethylaminocyclohexanol 492462-25-6P, 4-Benzyl-4-dimethylamino-1-[2-(3-fluorophenyl)ethyl]cyclohexanol 492462-26-7P, 4-Benzyl-4-dimethylamino-1-[2-(3-fluorophenyl)ethyl]cyclohexanol hydrochloride 492462-27-8P, 1-Benzyl-4-dimethylamino-4-(3-fluorobenzyl)cyclohexanol
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(analgesic; preparation of (amino)(arylalkyl)cyclohexanol analgesics starting from dioxaspiro[4.5]decanones, amines, and arylalkylmagnesium chlorides)

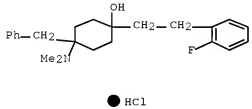
RN 492461-57-1 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(2-phenylethyl)-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



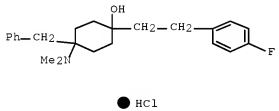
RN 492461-59-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1,4-bis(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



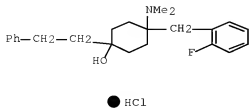
RN 492461-63-9 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(2-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



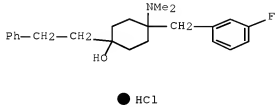
RN 492461-65-1 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



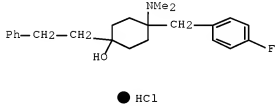
RN 492461-67-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(2-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



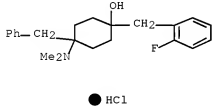
RN 492461-71-9 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(3-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



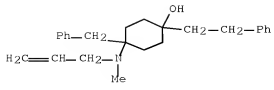
RN 492461-75-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(4-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



RN 492461-81-1 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[(2-fluorophenyl)methyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)

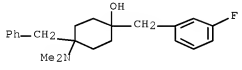


RN 492461-85-5 CAPLUS
CN Cyclohexanol, 4-(methyl-2-propenylamino)-1-(2-phenylethyl)-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



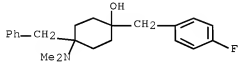
● HCl

RN 492461-94-6 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[(3-fluorophenyl)methyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



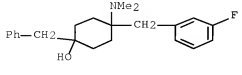
● HCl

RN 492461-98-0 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[(4-fluorophenyl)methyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



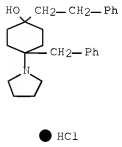
● HCl

RN 492462-03-0 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(3-fluorophenyl)methyl]-1-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



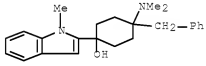
● HCl

RN 492462-05-2 CAPLUS
CN Cyclohexanol, 1-(2-phenylethyl)-4-(phenylmethyl)-4-(1-pyrrolidinyl)-, hydrochloride (9CI) (CA INDEX NAME)

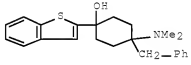


● HCl

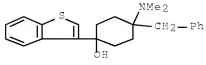
RN 492462-14-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(1-methyl-1H-indol-2-yl)-4-(phenylmethyl)- (CA INDEX NAME)



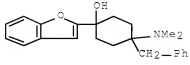
RN 492462-16-5 CAPLUS
CN Cyclohexanol, 1-benzo[b]thien-2-yl-4-(dimethylamino)-4-(phenylmethyl)- (CA INDEX NAME)



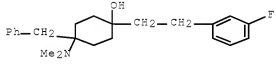
RN 492462-21-2 CAPLUS
CN Cyclohexanol, 1-benzo[b]thien-3-yl-4-(dimethylamino)-4-(phenylmethyl)- (CA INDEX NAME)



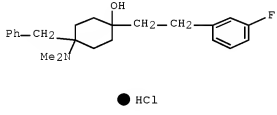
RN 492462-23-4 CAPLUS
CN Cyclohexanol, 1-(2-benzofuranyl)-4-(dimethylamino)-4-(phenylmethyl)- (CA INDEX NAME)



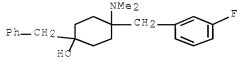
RN 492462-25-6 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(3-fluorophenyl)ethyl]-4-(phenylmethyl)- (CA INDEX NAME)



RN 492462-26-7 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(3-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



RN 492462-27-8 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-[(3-fluorophenyl)methyl]-1-(phenylmethyl)- (CA INDEX NAME)

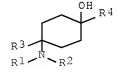


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:76741 CAPLUS Full-text
DOCUMENT NUMBER: 138:136953
TITLE: Preparation of substituted 4-aminocyclohexanols as regulators for the nociceptin/orphanin FQ ligand ORL-1 receptor system
INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-heinrich; Englberger, Werner; Wnendt, Stephan
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008370	A1	20030130	WO 2002-EP7842	20020715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10135636	A1	20030206	DE 2001-10135636	20010717
CA 2453901	A1	20030130	CA 2002-2453901	20020715
AU 2002321215	A1	20030303	AU 2002-321215	20020715
AU 2002321215	B2	20070802		
EP 1406858	A1	20040414	EP 2002-754882	20020715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 2004001082	A2	20040830	HU 2004-1082	20020715
JP 2004534858	T	20041118	JP 2003-513931	20020715
MX 2004PA00446	A	20040318	MX 2004-PA446	20040115
US 2004236104	A1	20041125	US 2004-758242	20040116
US 7183436	B2	20070227		

PRIORITY APPLN. INFO.: DE 2001-10135636 A 20010717
WO 2002-EP7842 W 20020715
OTHER SOURCE(S): MARPAT 138:136953
GI



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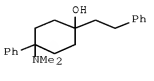


II

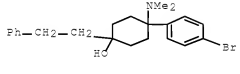
AB Title compds. I [R1-2 = H, alkyl, cycloalkyl, etc.; R3 = (hetero)aryl; R4 = cycloalkyl, (hetero)aryl, etc.] are prepared For instance, 1,4-dioxoaspiro[4.5]decan-8-one was converted to 8-dimethylamino-1,4-

dioxaspiro[4.5]decan-8-carbonitrile (MeOH, Me2NH, KCN). Displacement of this intermediate with phenylmagnesium chloride followed by deprotection and subsequent treatment with phenethylmagnesium chloride results in the formation of II. II has Ki = 4.4 nM for the ORL-1 receptor. I are useful for treating pain.

IT 108914-87-0P, 4-(4-Bromophenyl)-4-dimethylamino-1-phenethylcyclohexanol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(substituted 4-aminocyclohexanols as regulators for nociception/orphanin FQ ligand ORL-1 receptor system)

RN 108914-87-0 CAPLUS

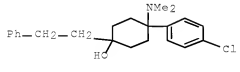
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)- (CA INDEX NAME)



IT 77253-95-3P, 4-(4-Chlorophenyl)-4-dimethylamino-1-phenethylcyclohexanol 108914-89-2P, 4-Dimethylamino-1-phenethyl-4-phenylcyclohexanol 492451-53-3P, 4-Dimethylamino-1-(1-methyl-1H-indol-2-yl)-4-phenylcyclohexanol 492451-54-4P, 1-[Benzo[b]thiophen-2-yl]-4-dimethylamino-4-phenylcyclohexanol 492451-55-5P, 1-[Benzo[b]thiophen-3-yl]-4-dimethylamino-4-phenylcyclohexanol 492451-56-6P, 1-(1-(Benzenesulfonyl)-1H-indol-2-yl)-4-dimethylamino-4-phenylcyclohexanol 492451-57-7P, 1-[Benzofuran-2-yl]-4-dimethylamino-4-phenylcyclohexanol 492451-58-8P, 1-[Benzothiazol-2-yl]-4-dimethylamino-4-phenylcyclohexanol 492451-59-9P, 4-Dimethylamino-1-phenethyl-4-phenylcyclohexanol hydrochloride 492451-60-2P, 4-(4-Chlorophenyl)-4-dimethylamino-1-phenethylcyclohexanol hydrochloride 492451-61-3P, 4-(4-Bromophenyl)-4-dimethylamino-1-phenethylcyclohexanol hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted 4-aminocyclohexanols as regulators for nociception/orphanin FQ ligand ORL-1 receptor system)

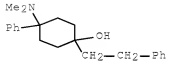
RN 77253-95-3 CAPLUS

CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)- (CA INDEX NAME)

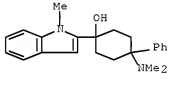


RN 108914-89-2 CAPLUS

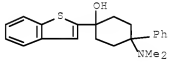
CN Cyclohexanol, 4-(dimethylamino)-4-phenyl-1-(2-phenylethyl)- (CA INDEX NAME)



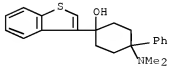
RN 492451-53-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(1-methyl-1H-indol-2-yl)-4-phenyl- (CA INDEX NAME)



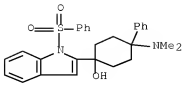
RN 492451-54-4 CAPLUS
CN Cyclohexanol, 1-benzo[b]thien-2-yl-4-(dimethylamino)-4-phenyl- (CA INDEX NAME)



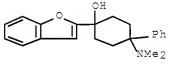
RN 492451-55-5 CAPLUS
CN Cyclohexanol, 1-benzo[b]thien-3-yl-4-(dimethylamino)-4-phenyl- (CA INDEX NAME)



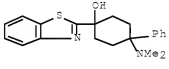
RN 492451-56-6 CAPLUS
CN 1H-Indole, 2-[4-(dimethylamino)-1-hydroxy-4-phenylcyclohexyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



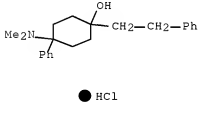
RN 492451-57-7 CAPLUS
CN Cyclohexanol, 1-(2-benzofuranyl)-4-(dimethylamino)-4-phenyl- (CA INDEX NAME)



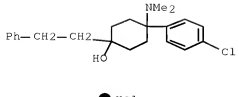
RN 492451-58-8 CAPLUS
CN Cyclohexanol, 1-(2-benzothiazolyl)-4-(dimethylamino)-4-phenyl- (CA INDEX NAME)



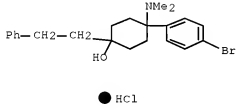
RN 492451-59-9 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-phenyl-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



RN 492451-60-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



RN 492451-61-3 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:851115 CAPLUS Full-text
DOCUMENT NUMBER: 136:5907
TITLE: Synthesis of aryl-amido-cyclohexane derivatives and their use as NK-1 receptor antagonists
INVENTOR(S): Castro Pineiro, Jose Luis; Dinnell, Kevin; Elliott, Jason Matthew; Hollingworth, Gregory John; Shaw, Duncan Edward; Swain, Christopher John
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087839	A1	20011122	WO 2001-GB2145	20010516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2408849	A1	20011122	CA 2001-2408849	20010516

EP 1286967	A1	20030305	EP 2001-929829		20010516
EP 1286967	B1	20060927			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003533509	T	20031111	JP 2001-584234		20010516
AT 340781	T	20061015	AT 2001-929829		20010516
ES 2273837	T3	20070516	ES 2001-929829		20010516
US 2003236250	A1	20031225	US 2002-276127		20021113
US 7105507	B2	20060912			
PRIORITY APPLN. INFO.:			GB 2000-12240	A	20000519
			WO 2001-GB2145	W	20010516

OTHER SOURCE(S): MARPAT 136:5907

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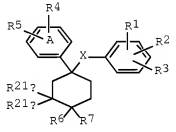

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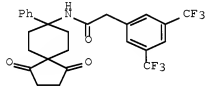


II

AB Title compds. I [ring A = Ph or pyridyl; X = linker selected from amido(carbonyl), amino, ester, ether; R1 = OH, (fluoro)alkyl, alkenyl, cycloalkyl, (fluoro)alkoxy, etc.; R2 = H, halo, alkyl, alkoxy or R1-2 with the atom to which they are attached, may form a 5 - 6 membered ring; R3 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, cycloalkyl, CN, etc. or R3 = 5 - 6 membered heterocyclic ring; R4 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, OH, NO2, CN, etc.; R5 = H, halo, (fluoro)alkyl, alkoxy; R6 = H, OH, alkyl; R7 = H, OH, alkylamino, alkylcarboxy, carbocyclyl, C-linked heterocyclyl or heteroaryl or R6-7 together represent :O, :CH-ester, ketal; R21a = H, halo, OH; R21b = H, or R21a-21b = F or together represent :O] were prepared Over 300 synthetic examples were disclosed. For instance, 3,5-bis(trifluoromethyl)benzeneacetic acid was converted to the acid chloride derivative (CH2Cl2, ClCOCOCl, DMF, room temperature, 1 h), and used to acylate 1,4-dioxo-8-phenylspiro[4.5]decan-8-amine (preparation given, dichloroethane, Et3N, room temperature) to give II as a brown gum in quant. yield. I are neurokinin 1 (NK-1) receptor antagonists (no data). Compds. I are of particular use in the treatment or prevention of depression, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia.

IT 374794-00-0P

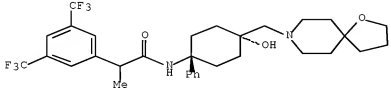
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of aryl-amido-cyclohexane derivs. and use as NK-1 receptor antagonists)

RN 374794-00-0 CAPLUS

CN Benzeneacetamide, N-[cis-4-[(4-hydroxy-1-oxa-8-azaspiro[4.5]dec-8-yl)methyl]-1-phenylcyclohexyl]-α-methyl-3,5-bis(trifluoromethyl)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:713343 CAPLUS Full-text

DOCUMENT NUMBER: 135:272894

TITLE: Preparation of β-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-α

INVENTOR(S): Duan, Jingwu; King, Bryan W.; Decicco, Carl; Maduskuie, Thomas P., Jr.; Voss, Matthew E.

PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA

SOURCE: PCT Int. Appl., 483 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070734	A2	20010927	WO 2001-US8336	20010315
WO 2001070734	A3	20020314		
W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, NZ, PL, PT, RO, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2400168	A1	20010927	CA 2001-2400168	20010315
AU 2001050850	A	20011003	AU 2001-50850	20010315
EP 1263756	A2	20021211	EP 2001-924171	20010315
EP 1263756	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
BR 2001009469	A	20030429	BR 2001-9469	20010315
JP 2003528097	T	20030924	JP 2001-568935	20010315
AT 260272	T	20040315	AT 2001-924171	20010315
NZ 521245	A	20040430	NZ 2001-521245	20010315
ES 2215893	T3	20041016	ES 2001-924171	20010315
US 2002013341	A1	20020131	US 2001-811116	20010316
US 6495565	B2	20021217		

IN 2002MN01075	A	20050304	IN 2002-MN1075		20020808
HK 1049334	A1	20040716	HK 2003-101437		20030226
PRIORITY APPLN. INFO.:			US 2000-190183P	P	20000317
			US 2000-235467P	P	20000926
			US 2000-252062P	P	20001120
			WO 2001-US8336	W	20010315

OTHER SOURCE(S): MARPAT 135:272894

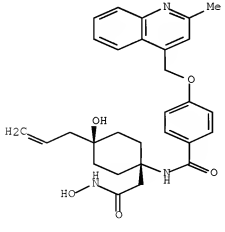
AB Novel β-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 [Ra1 = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ra1 may form a ring], CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRa1)r1O(CRaRa1)r-Q (r, r1 = 0-4), (CRaRa1)r1NRa(CRaRa1)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRa1)r1O(CRaRa1)r-Q1, (CRaRa1)r1NRa(CRaRa1)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepared as metalloprotease and TNF-α inhibitors. Thus, N-hydroxy-1-[[4-[(2- methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepared by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

IT 362701-92-6P 362701-93-7P 362702-25-8P
362702-26-9P 362702-37-2P 362702-38-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

RN 362701-92-6 CAPLUS

CN Benzamide, N-[trans-4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(2-propenyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (9CI) (CA INDEX NAME)

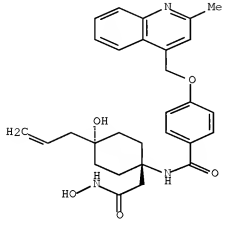
Relative stereochemistry.



RN 362701-93-7 CAPLUS

CN Benzamide, N-[cis-4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(2-propenyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (9CI) (CA INDEX NAME)

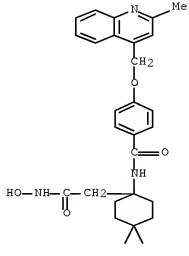
Relative stereochemistry.



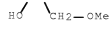
RN 362702-25-8 CAPLUS

CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(methoxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

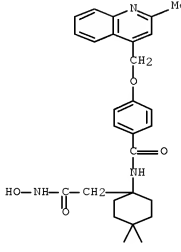


RN 362702-26-9 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(methoxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

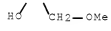
CM 1

CRN 362702-25-8
CMF C28 H33 N3 O6

PAGE 1-A



PAGE 2-A

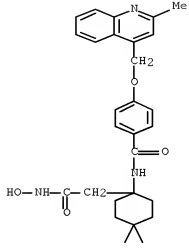


CM 2

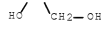
CRN 76-05-1
CMF C2 H F3 O2

RN 362702-37-2 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(hydroxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

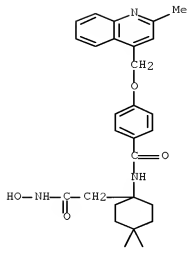


RN 362702-38-3 CAPLUS
CN Benzamide, N-[4-hydroxy-1-[2-(hydroxyamino)-2-oxoethyl]-4-(hydroxymethyl)cyclohexyl]-4-[(2-methyl-4-quinolinyl)methoxy]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

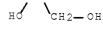
CM 1

CRN 362702-37-2
CMF C27 H31 N3 O6

PAGE 1-A



PAGE 2-A



CM 2

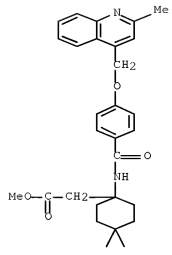
CRN 76-05-1
CMF C2 H F3 O2

IT 362706-44-3P 362706-61-4P 362706-62-5P
362706-67-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

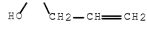
RN 362706-44-3 CAPLUS

CN Cyclohexaneacetic acid, 4-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-4-(2-propenyl)-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

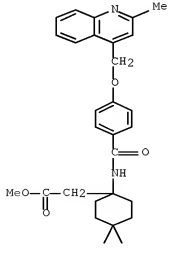


PAGE 2-A

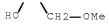


RN 362706-61-4 CAPLUS
CN Cyclohexaneacetic acid, 4-hydroxy-4-(methoxymethyl)-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, methyl ester (CA INDEX NAME)

PAGE 1-A

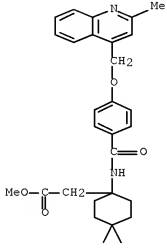


PAGE 2-A

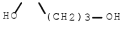


RN 362706-62-5 CAPLUS
CN Cyclohexaneacetic acid, 4-hydroxy-4-(3-hydroxypropyl)-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, methyl ester (CA INDEX NAME)

PAGE 1-A

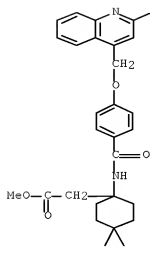


PAGE 2-A

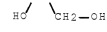


RN 362706-67-0 CAPLUS
CN Cyclohexaneacetic acid, 4-hydroxy-4-(hydroxymethyl)-1-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, methyl ester (CA INDEX NAME)

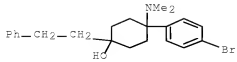
PAGE 1-A



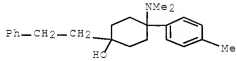
PAGE 2-A



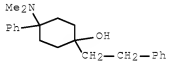
L5 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:423027 CAPLUS Full-text
DOCUMENT NUMBER: 107:23027
ORIGINAL REFERENCE NO.: 107:3886h,3887a
TITLE: Synthesis of some cyclohexanol derivatives
AUTHOR(S): Swahn, B. M.; Trogen, L.
CORPORATE SOURCE: Foersvarets Forskningsanst., Umea, Swed.
SOURCE: Report (1985), FOA-C-40220-C1; Order No. PB86-129921/GAR, 21 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1986, 86(7), Abstr. No. 613,507
DOCUMENT TYPE: Report
LANGUAGE: Swedish
AB Some substances with analgesic properties, e.g., 4-(p-bromophenyl)-4-(dimethylamino)-1-(phenylethyl)cyclohexanol, 4-(dimethylamino)-4-(p-methylphenyl)-1-(phenylethyl)cyclohexanol, 4-(dimethylamino)-4-phenyl-1-(phenylethyl)clohexanol, and 4-(N-butyl-N-methylamino)-4-(p-methylphenyl)- 1-(phenylethyl)cyclohexanol were prepared
IT 108914-87-0P 108914-88-1P 108914-89-2P 108914-90-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 108914-87-0 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)- (CA INDEX NAME)



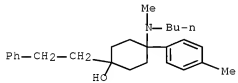
RN 108914-88-1 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-phenylethyl)- (CA INDEX NAME)



RN 108914-89-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-phenyl-1-(2-phenylethyl)- (CA INDEX NAME)

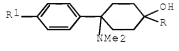


RN 108914-90-5 CAPLUS
CN Cyclohexanol, 4-(butylmethylamino)-4-(4-methylphenyl)-1-(2-phenylethyl)- (CA INDEX NAME)



L5 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:605548 CAPLUS Full-text
DOCUMENT NUMBER: 103:205548
ORIGINAL REFERENCE NO.: 103:32977a,32980a
TITLE: Quantitative correlation between hydrophobicity and analgesic activity of 4-amino-4-arylcyclohexanols
AUTHOR(S): Rao, M. N. A.; Rao, S. Chakradhara
CORPORATE SOURCE: Coll. Pharm., Kasturba Med. Coll., Manipal, 576119, India

SOURCE: Indian Drugs (1985), 22(5), 252-7
CODEN: INDRBA; ISSN: 0019-462X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



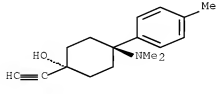
I

AB A quant. structure-activity relationship was established between hydrophobicity and analgesic activity of 39 4-amino-4-arylcyclohexanol derivs. (I; R = H, alkyl, or aralkyl; R1 = H, Cl, Br, or Me), which are some of the most potent opioids reported to date. Trans conformation and hydrophobicity of the substituents at the C atom possessing the OH group in the cyclohexanol nucleus were most important for the activity. The equations obtained on the data from the tail-flick test and the HCl-induced writhing test were very similar, showing that a common mechanism is involved in both methods.

IT 70894-79-0 70894-80-3 70894-81-4
70894-88-1 70894-91-6 70895-00-0
70936-62-8 76825-07-5 76825-10-0
77239-98-6 77239-99-7 99289-40-4
99289-41-5 99289-42-6 99289-43-7
99289-44-8 99289-45-9 99289-46-0
99289-47-1 99289-48-2 99289-49-3
99289-50-6 99289-51-7 99289-52-8
99289-53-9 99289-54-0 99289-55-1
99289-56-2 99289-57-3 99289-58-4
99289-59-5 99289-60-8 99300-35-3
99300-36-4
RL: BIOL (Biological study)
(analgesia from, hydrophobicity and structure in relation to)

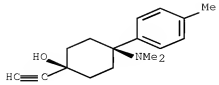
RN 70894-79-0 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-ethynyl-4-(4-methylphenyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



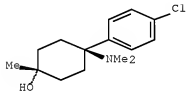
RN 70894-80-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-ethynyl-4-(4-methylphenyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.



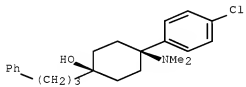
RN 70894-81-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



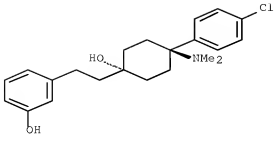
RN 70894-88-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.



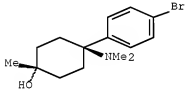
RN 70894-91-6 CAPLUS
CN Phenol, 3-[2-[4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxycyclohexyl]ethyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



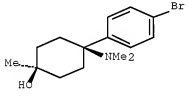
RN 70895-00-0 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



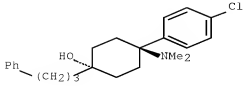
RN 70936-62-8 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-methyl-, cis- (CA INDEX NAME)

Relative stereochemistry.



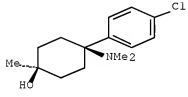
RN 76825-07-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



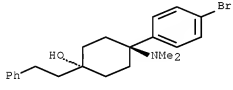
RN 76825-10-0 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-methyl-, cis- (CA INDEX NAME)

Relative stereochemistry.



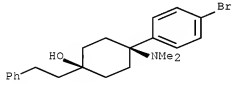
RN 77239-98-6 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



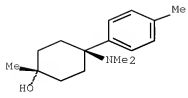
RN 77239-99-7 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.



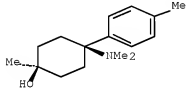
RN 99289-40-4 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-methyl-4-(4-methylphenyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



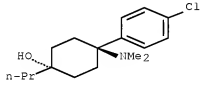
RN 99289-41-5 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-methyl-4-(4-methylphenyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.



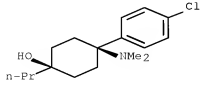
RN 99289-42-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



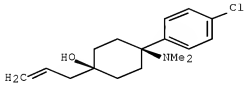
RN 99289-43-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl-, cis- (CA INDEX NAME)

Relative stereochemistry.



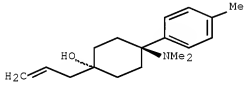
RN 99289-44-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-propenyl)-, cis-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



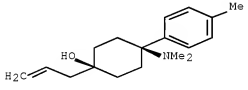
RN 99289-45-9 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-propenyl)-, trans-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



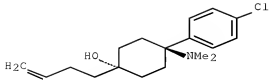
RN 99289-46-0 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-propenyl)-, cis-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



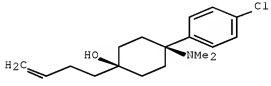
RN 99289-47-1 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)-, trans-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



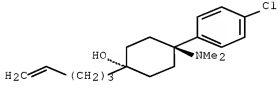
RN 99289-48-2 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)-, cis-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



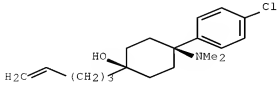
RN 99289-49-3 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)-, trans-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 99289-50-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)-, cis-
(9CI) (CA INDEX NAME)

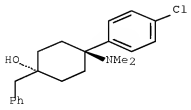
Relative stereochemistry.



RN 99289-51-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)-,

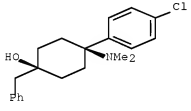
trans- (CA INDEX NAME)

Relative stereochemistry.



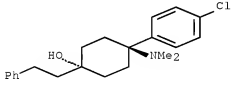
RN 99289-52-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)-, cis-
(CA INDEX NAME)

Relative stereochemistry.



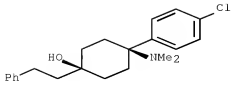
RN 99289-53-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-,
trans- (CA INDEX NAME)

Relative stereochemistry.



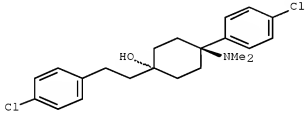
RN 99289-54-0 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-,
cis- (CA INDEX NAME)

Relative stereochemistry.



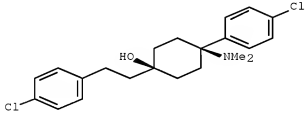
RN 99289-55-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethyl]-4-(dimethylamino)-, trans- (CA INDEX NAME)

Relative stereochemistry.



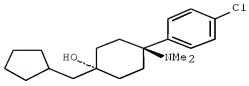
RN 99289-56-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethyl]-4-(dimethylamino)-, cis- (CA INDEX NAME)

Relative stereochemistry.



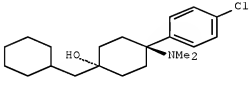
RN 99289-57-3 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(cyclopentylmethyl)-4-(dimethylamino)-, trans- (CA INDEX NAME)

Relative stereochemistry.



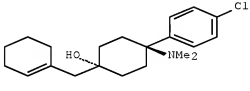
RN 99289-58-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(cyclohexylmethyl)-4-(dimethylamino)-, trans- (CA INDEX NAME)

Relative stereochemistry.



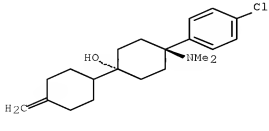
RN 99289-59-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(1-cyclohexen-1-ylmethyl)-4-(dimethylamino)-, trans- (CA INDEX NAME)

Relative stereochemistry.



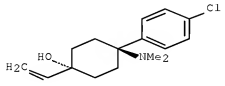
RN 99289-60-8 CAPLUS
CN [1,1'-Bicyclohexyl]-1-ol, 4-(4-chlorophenyl)-4-(dimethylamino)-4'-methylene-, trans- (CA INDEX NAME)

Relative stereochemistry.



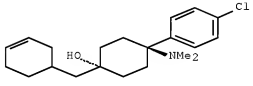
RN 99300-35-3 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-ethenyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



RN 99300-36-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(3-cyclohexen-1-ylmethyl)-4-(dimethylamino)-, trans- (CA INDEX NAME)

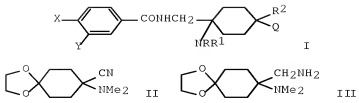
Relative stereochemistry.



L5 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:615791 CAPLUS Full-text
DOCUMENT NUMBER: 97:215791
ORIGINAL REFERENCE NO.: 97:36212h,36213a
TITLE: Benzamide derivative analgesics
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4346101	A	19820824	US 1980-213963	19801208
PRIORITY APPLN. INFO.:			US 1980-213963	19801208

OTHER SOURCE(S): CASREACT 97:215791; MARPAT 97:215791
GI



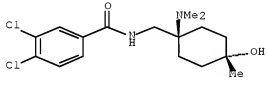
AB Benzamides [I; R, R1 = C1-3 alkyl; R2 = PhCH2, Me; Q = H, OH; (R2Q) = O(CH2)2O, O(CH2)3O, O(CH2CR3R4CH2)O, R3 = R4 = Me; R3 = H, R4 = Me; X = halo, CF3, C1-3 alkoxy, NO2; Y = halo, H] were prepared Thus, II was reduced with LiAlH4 to give III which was treated with 3,4-Cl2C6H3COCl in THF/Et3N to give I [R = R1 = Me; (R2Q) = O(CH2)2O; X = Y = Cl (IV)]. A sterile aqueous dispersion suitable for i.m. injection and containing in each mL 25 mg of IV as the essential active ingredient was described.

IT 83631-93-0P 83631-94-1P 83631-96-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 83631-93-0 CAPLUS

CN Benzamide, 3,4-dichloro-N-[[1-(dimethylamino)-4-hydroxy-4-methylcyclohexyl]methyl]-, trans- (9CI) (CA INDEX NAME)

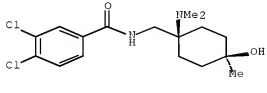
Relative stereochemistry.



RN 83631-94-1 CAPLUS

CN Benzamide, 3,4-dichloro-N-[[1-(dimethylamino)-4-hydroxy-4-methylcyclohexyl]methyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

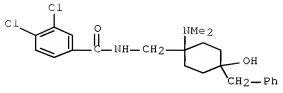


RN 83631-96-3 CAPLUS

CN Benzamide, 3,4-dichloro-N-[[1-(dimethylamino)-4-hydroxy-4-(phenylmethyl)cyclohexyl]methyl]-, mono(4-methylbenzenesulfonate) (salt) (9CI) (CA INDEX NAME)

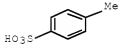
CM 1

CRN 83631-95-2
CMF C23 H28 Cl2 N2 O2

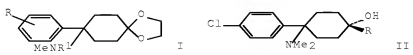


CM 2

CRN 104-15-4
CMF C7 H8 O3 S



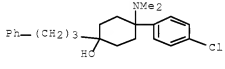
L5 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:150032 CAPLUS Full-text
DOCUMENT NUMBER: 94:150032
ORIGINAL REFERENCE NO.: 94:24387a,24390a
TITLE: 4-Aryl-4-aminocyclohexanone derivatives: a chemically novel series of analgesics including opioid antagonists and extremely potent agonists
AUTHOR(S): VonVoigtlander, Philip F.; Lednicer, Daniel; Lewis, Richard A.; Gay, David D.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Endog. Exog. Opiate Agonists Antagonists, Proc. Int. Narc. Res. Club Conf. (1980), Meeting Date 1979, 17-21. Editor(s): Way, E. Leong. Pergamon: Elmsford, N. Y.
CODEN: 45EWA5
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



AB A structurally novel series of opioids was characterized biol. These compds. are all derivs. of phenylcyclohexylamine I where R = Me, CMe3, or halo; R1 = Me, Pr, Bu, pentyl, or CH2CH:CH2, or II where R = alkyl, alkylphenyl, etc.). The structure-activity relationships (SAR's) of this series are discussed as they pertain to the effects of Ph substitutions, substitution in the 1 position of the cyclohexanone and alterations in the N substitution. Biol. characterization includes in vivo analgesia, narcotic antagonism and narcotic behavioral effects, and in vitro 3H-naloxone binding inhibition. Examination of these in vivo and in vitro SAR data suggests that p-halo substitutions optimize the ability of the compds. to gain access to the analgesic receptors, whereas m-OH substitution induced narcotic antagonist activity. The degree of antagonist activity may be decreased by lengthening the aminoalkyl substitution from Me to pentyl. Remarkable increases in analgesic and 3H-naloxone binding potency are induced by addition of a phenylethyl moiety to the 1 position of the cyclohexanone. These compds. have in vivo analgesic potencies up to 12,000 times that of morphine. Conformational commonalities between these latter compds. and the enkephalins are discussed.

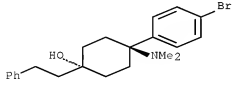
IT 77239-97-5 77239-98-6 77239-99-7
77253-89-5 77253-90-8 77253-91-9
77253-92-0 77253-93-1 77253-94-2
77253-95-3
RL: BIOL (Biological study)
(analgesic and narcotic antagonist activities of, structure in relation to)

RN 77239-97-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)- (CA INDEX NAME)



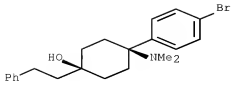
RN 77239-98-6 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.

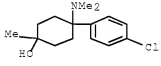


RN 77239-99-7 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, cis- (CA INDEX NAME)

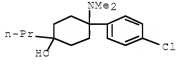
Relative stereochemistry.



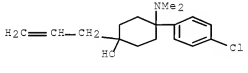
RN 77253-89-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-methyl- (CA INDEX NAME)



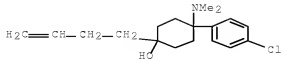
RN 77253-90-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl- (CA INDEX NAME)



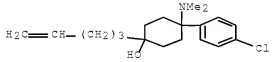
RN 77253-91-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-propenyl)- (9CI) (CA INDEX NAME)



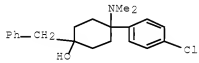
RN 77253-92-0 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



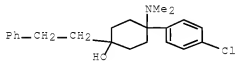
RN 77253-93-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)- (9CI) (CA INDEX NAME)



RN 77253-94-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)- (CA INDEX NAME)

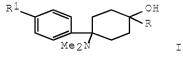


RN 77253-95-3 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)- (CA INDEX NAME)



L5 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:139370 CAPLUS Full-text
DOCUMENT NUMBER: 94:139370
ORIGINAL REFERENCE NO.: 94:22809a,22812a
TITLE: 4-Amino-4-arylcyclohexanones and their derivatives: a novel class of analgesics. 2. Modification of the carbonyl function
AUTHOR(S): Lednicer, Daniel; VonVoigtlander, Philip F.; Emmert, D. Edward
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, USA
SOURCE: Journal of Medicinal Chemistry (1981), 24(4), 404-8

CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 94:139370
GI



I

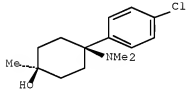
AB The cyclohexanols I (R = H, alkyl, alkenyl, alkynyl, PhCH2, PhCH2CH2, etc.; R1 = H, Cl, Br, Me), prepared by the reduction of or addition of nucleophiles to the corresponding cyclohexanones, were separated into cis and trans isomers and tested for analgesic activity. The trans (OH and N) isomers were invariably more potent than the cis. I (R = PhCH2CH2) are among the most potent opioids reported to date; possibly the ring system may be providing an addnl. binding site for these compds., and thus greatly enhance their affinity for the opioid receptor.

IT 76825-10-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(analgesic, narcotic, and sedative activity of)

RN 76825-10-0 CAPLUS

CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-methyl-, cis- (CA INDEX NAME)

Relative stereochemistry.

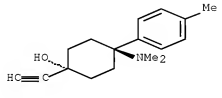


IT 70894-79-0P 70894-80-3P 70894-81-4P
70894-82-5P 70894-83-6P 70894-84-7P
70894-85-8P 70894-86-9P 70894-89-2P
70894-90-5P 70894-91-6P 70894-92-7P
70894-93-8P 70894-94-9P 70894-95-0P
70894-96-1P 70894-97-2P 70894-98-3P
70894-99-4P 70895-00-0P 70895-01-1P
70895-02-2P 70895-03-3P 70895-04-4P
70895-05-5P 70895-06-6P 70895-13-5P
70895-14-6P 70895-15-7P 70895-16-8P
70895-17-9P 70895-18-0P 70895-19-1P
70895-20-4P 70895-21-5P 70910-82-6P
70936-62-8P 76825-07-5P 76825-08-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic activity of)

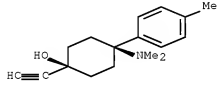
RN 70894-79-0 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-ethynyl-4-(4-methylphenyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



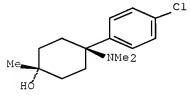
RN 70894-80-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-ethynyl-4-(4-methylphenyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.



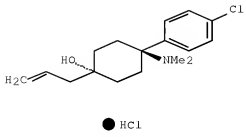
RN 70894-81-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



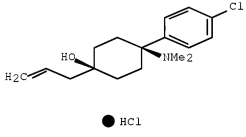
RN 70894-82-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



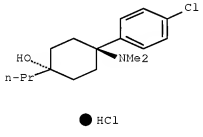
RN 70894-83-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



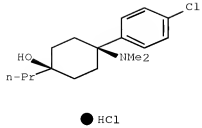
RN 70894-84-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



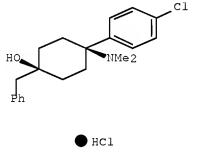
RN 70894-85-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



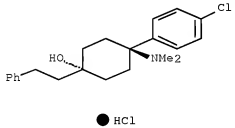
RN 70894-86-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



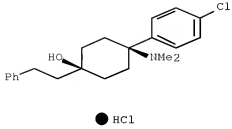
RN 70894-89-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



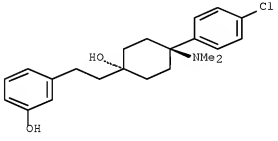
RN 70894-90-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



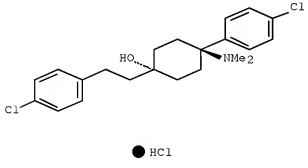
RN 70894-91-6 CAPLUS
CN Phenol, 3-[2-[4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxycyclohexyl]ethyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



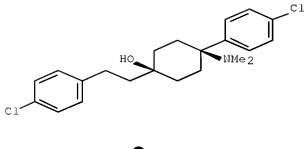
RN 70894-92-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethyl]-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



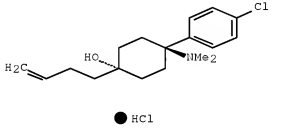
RN 70894-93-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethyl]-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



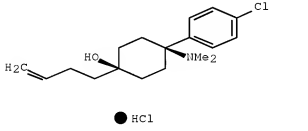
RN 70894-94-9 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



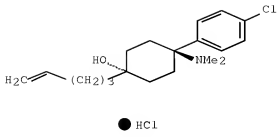
RN 70894-95-0 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



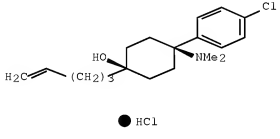
RN 70894-96-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



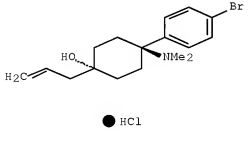
RN 70894-97-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



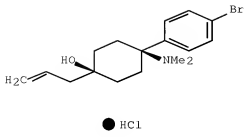
RN 70894-98-3 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



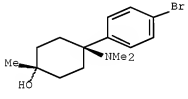
RN 70894-99-4 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



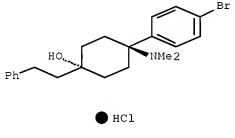
RN 70895-00-0 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



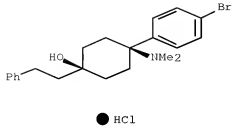
RN 70895-01-1 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



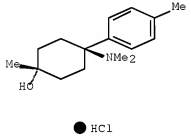
RN 70895-02-2 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



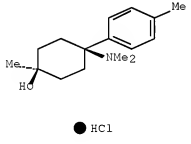
RN 70895-03-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-methyl-4-(4-methylphenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



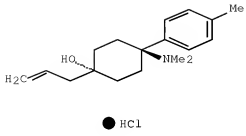
RN 70895-04-4 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-methyl-4-(4-methylphenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



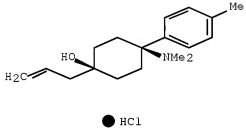
RN 70895-05-5 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-propenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



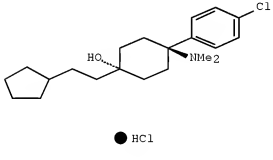
RN 70895-06-6 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-propenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



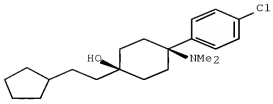
RN 70895-13-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclopentylethyl)-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



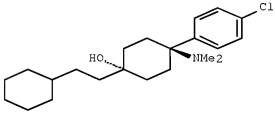
RN 70895-14-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclopentylethyl)-4-(dimethylamino)-, cis- (CA INDEX NAME)

Relative stereochemistry.



RN 70895-15-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclohexylethyl)-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

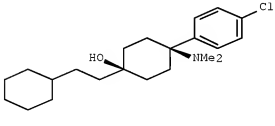
Relative stereochemistry.



● HCl

RN 70895-16-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclohexylethyl)-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

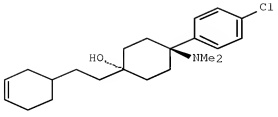
Relative stereochemistry.



● HCl

RN 70895-17-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(3-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

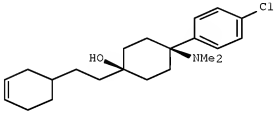
Relative stereochemistry.



● HCl

RN 70895-18-0 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(3-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

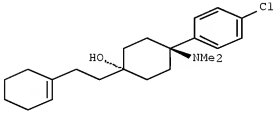
Relative stereochemistry.



● HCl

RN 70895-19-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(1-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

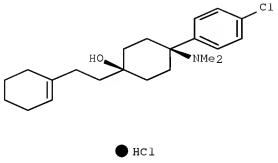
Relative stereochemistry.



● HCl

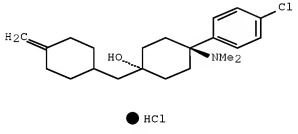
RN 70895-20-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(1-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



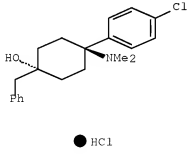
RN 70895-21-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-[(4-methylenecyclohexyl)methyl]-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



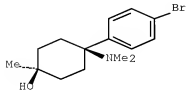
RN 70910-82-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



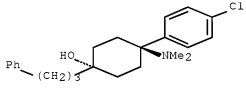
RN 70936-62-8 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-methyl-, cis- (CA INDEX NAME)

Relative stereochemistry.



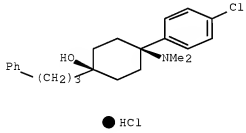
RN 76825-07-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



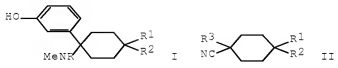
RN 76825-08-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:120935 CAPLUS Full-text
DOCUMENT NUMBER: 94:120935
ORIGINAL REFERENCE NO.: 94:19763a,19766a
TITLE: 4-Aryl-4-aminocyclohexanones and their derivatives, a novel class of analgesics. 3. m-Hydroxyphenyl derivatives
AUTHOR(S): Lednicer, Daniel; Von Voigtlander, Philip F.; Emmert, D. Edward
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA

SOURCE: Journal of Medicinal Chemistry (1981), 24(3), 341-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 94:120935
GI

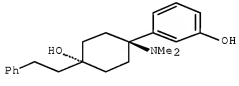


AB Title compds. I [R = Me, allyl, Bu, CH2CHMe2, cyclopropylmethyl, Me(CH2)4, PhOCH2CH2; R1R2 = OCH2CH2O, O(CH2)3O, OCH2CMe2CH2O, OCH2CH(CHCH:CH2)CH2O, OCH2CHPhCH2O, O; R1 = OH, R2 = H, Me, PhCH2, PhCH2CH2, 4-ClC6H4CH2CH2] were prepared by Grignard reaction of II (R3 = NH2) with 3-ThpOC6H4Br (Thp = 2-tetrahydropyranyl). I (R1R2 = OCH2CH2O) had narcotic antagonist activity. Aminoalcs. I (R1 = HO, R2 = PhCH2, PhCH2CH2, 4-ClC6H4CH2CH2) which were prepared by the Grignard reaction of I (R1R2 = O) with R2Cl were potent analgesics but had no antagonist activity.

IT 70895-07-7P 70895-08-8P 70895-09-9P
70895-11-3P 70895-12-4P 76626-22-7P
76626-23-8P 76626-24-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic activity of)

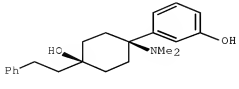
RN 70895-07-7 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(2-phenylethyl)cyclohexyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



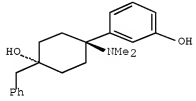
RN 70895-08-8 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(2-phenylethyl)cyclohexyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



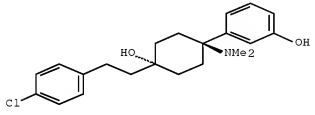
RN 70895-09-9 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(phenylmethyl)cyclohexyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



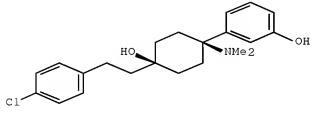
RN 70895-11-3 CAPLUS
CN Phenol, 3-[4-[2-(4-chlorophenyl)ethyl]-1-(dimethylamino)-4-hydroxycyclohexyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 70895-12-4 CAPLUS
CN Phenol, 3-[4-[2-(4-chlorophenyl)ethyl]-1-(dimethylamino)-4-hydroxycyclohexyl]-, cis- (9CI) (CA INDEX NAME)

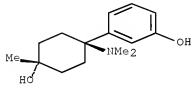
Relative stereochemistry.



RN 76626-22-7 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-methylcyclohexyl]-, trans- (9CI)

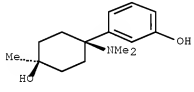
(CA INDEX NAME)

Relative stereochemistry.



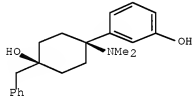
RN 76626-23-8 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-methylcyclohexyl]-, cis- (9CI)
(CA INDEX NAME)

Relative stereochemistry.



RN 76626-24-9 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(phenylmethyl)cyclohexyl]-, cis-
(9CI) (CA INDEX NAME)

Relative stereochemistry.

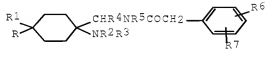


L5 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:604303 CAPLUS Full-text
DOCUMENT NUMBER: 93:204303
ORIGINAL REFERENCE NO.: 93:32585a,32588a
TITLE: Phenylacetamide derivative analgesics
INVENTOR(S): Lednicer, Daniel; Szmuszkovicz, Jacob
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4212878	A	19800715	US 1978-872632	19780126
PRIORITY APPLN. INFO.:			US 1978-872632 A	19780126

OTHER SOURCE(S): MARPAT 93:204303
GI



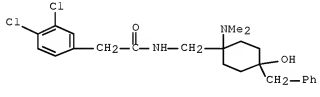
I

AB Treating phenylacetic acids with 1-aminomethyl-1- (dialkylamino)cyclohexanes gave amides I [RR1 = O, alkylenedioxy, or one of R and R1 is OH and the other is H, alkyl, phenylalkyl; R2, R3 = alkyl, R2 = 2-alkenyl and R3 = alkyl, or NR2R3 = heterocyclyl; R4 = H, alkyl; R5 = H, alkyl; R6, R7 = H, alkyl, alkoxy, halo (atomic number 9-35), NO2, CF3, N3], useful as analgesics (no data). Thus, coupling 3,4-C12C6H3CH2CO2H with 4-aminomethyl-4-pyrrolidinocyclohexanone ethylene ketal in the presence of carbonyldiimidazole gave 40% I [RR1 = OCH2CH2O, R2R3 = (CH2)4, R4 = R5 = H, R6 = 3-Cl, R7 = 4-Cl].

IT 75489-39-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 75489-39-3 CAPLUS

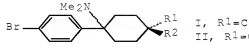
CN Benzeneacetamide, 3,4-dichloro-N-[[1-(dimethylamino)-4-hydroxy-4-(phenylmethyl)cyclohexyl]methyl]- (CA INDEX NAME)



L5 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	1979:551334 CAPLUS Full-text
DOCUMENT NUMBER:	91:151334
ORIGINAL REFERENCE NO.:	91:24285a,24288a
TITLE:	4-(p-Bromophenyl)-4-(dimethylamino)-1-phenethylcyclohexanol, an extremely potent representative of a new analgesic series
AUTHOR(S):	Lednicer, Daniel; VonVoigtlander, Philip F.
CORPORATE SOURCE:	Res. Lab., Upjohn Co., Kalamazoo, MI, 49002, USA
SOURCE:	Journal of Medicinal Chemistry (1979), 22(10), 1157-8 CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:	Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 91:151334
GI



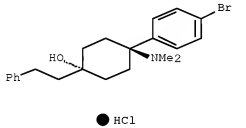
I, R^1=CH_2CH_2Ph, R^2=OH
II, R^1=OH, R^2=CH_2CH_2Ph

AB trans-4-(p-Bromophenyl)-4-(dimethylamino)-1-phenethylcyclohexanol-HCl (I-HCl) [70895-01-1] and its cis analog (II) [70895-02-2] were prepared from 1,4-dioxaspiro[4.5]decan-8-one [4746-97-8]. In analgesia tests on mice I showed a potency increment of 104 over that of morphine. Apparently, I conforms to the steric and bonding requirements of the analgesic opioid receptor. II was less effective.

IT 70895-01-1P 70895-02-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic activity of)

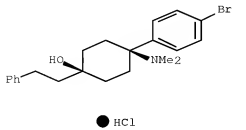
RN 70895-01-1 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 70895-02-2 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

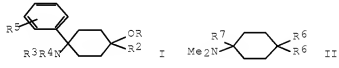
Relative stereochemistry.



L5 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:474328 CAPLUS Full-text
DOCUMENT NUMBER: 91:74328
ORIGINAL REFERENCE NO.: 91:12009a,12012a
TITLE: 4-Aminocyclohexanols, their acylates and acid addition salts
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: Ger. Offen., 58 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2839891	A1	19790412	DE 1978-2839891	19780913
US 4366172	A	19821228	US 1977-837510	19770929
GB 2005266	A	19790419	GB 1978-38272	19780927
GB 2005266	B	19820203		
FR 2404625	A1	19790427	FR 1978-27780	19780928
FR 2404625	B1	19811224		
JP 54059263	A	19790512	JP 1978-120333	19780929
CH 635818	A5	19830429	CH 1978-10157	19780929
PRIORITY APPLN. INFO.:			US 1977-837510 A	19770929
OTHER SOURCE(S):	MARPAT 91:74328			

GI



I II

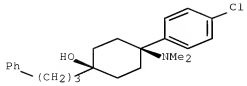
AB Aminocyclohexanols I [R = H, R1CO (R1 = C1-3 alkyl); R2 = H, C1-6 aliphatic group, cycloalkylalkyl (optionally unsatd.), (substituted) phenylalkyl; R3, R4 = C1-5 alkyl; R5 = H, halo, OH, C1-3 alkyl in meta or para position] and their physiol. acceptable salts, useful as analgesics (no data) were prepared Thus, 4-hydroxycyclohexanone was successively acetalized with (HOCH2)2, 4-hydroxycyclohexanone ethylene ketal oxidized with CrO3 (91% yield), 1,4-cyclohexanedione mono(ethylene ketal) cyanated with KCN and aminated with Me2NH.HCl (78% yield), nitrile II (R6R6 = OCH2CH2O, R7 = cyano) treated with 4-ClC6H4MgBr (34% yield), phenylcyclohexanone ketal II (R6R6 = OCH2CH2O, R7 = 4-ClC6H4) hydrolyzed with 2N HCl in MeOH (70% yield), and ketone II (R6R6 = O, R7 = 4-ClC6H4) reduced with NaBH4 to give 30% cyclohexanol I (R = R2 = H, R3 = R4 = Me, R5 = 4-Cl).

IT 70894-88-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as analgesic)

RN 70894-88-1 CAPLUS

CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.

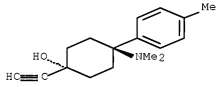


IT 70894-79-0P 70894-80-3P 70894-81-4P
70894-82-5P 70894-83-6P 70894-84-7P
70894-85-8P 70894-86-9P 70894-87-0P
70894-89-2P 70894-90-5P 70894-91-6P
70894-92-7P 70894-93-8P 70894-94-9P
70894-95-0P 70894-96-1P 70894-97-2P
70894-98-3P 70894-99-4P 70895-00-0P
70895-01-1P 70895-02-2P 70895-03-3P
70895-04-4P 70895-05-5P 70895-06-6P
70895-07-7P 70895-08-8P 70895-09-9P
70895-10-2P 70895-11-3P 70895-12-4P
70895-13-5P 70895-14-6P 70895-15-7P
70895-16-8P 70895-17-9P 70895-18-0P
70895-19-1P 70895-20-4P 70895-21-5P
70895-22-6P 70895-33-9P 70895-34-0P
70895-35-1P 70910-82-6P 70936-62-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 70894-79-0 CAPLUS

CN Cyclohexanol, 4-(dimethylamino)-1-ethynyl-4-(4-methylphenyl)-, trans- (CA INDEX NAME)

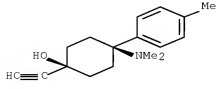
Relative stereochemistry.



RN 70894-80-3 CAPLUS

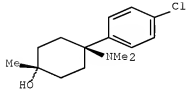
CN Cyclohexanol, 4-(dimethylamino)-1-ethynyl-4-(4-methylphenyl)-, cis- (CA INDEX NAME)

Relative stereochemistry.



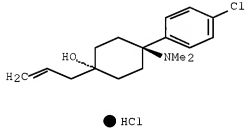
RN 70894-81-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



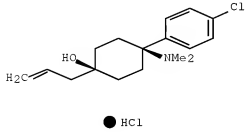
RN 70894-82-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 70894-83-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

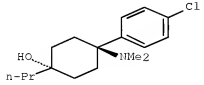
Relative stereochemistry.



RN 70894-84-7 CAPLUS

CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl-, hydrochloride, trans- (9CI) (CA INDEX NAME)

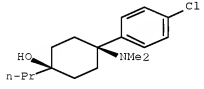
Relative stereochemistry.



● HCl

RN 70894-85-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-propyl-, hydrochloride, cis- (9CI) (CA INDEX NAME)

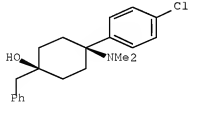
Relative stereochemistry.



● HCl

RN 70894-86-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

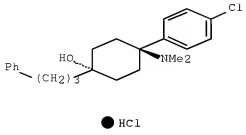
Relative stereochemistry.



● HCl

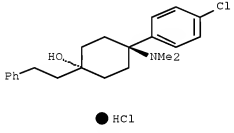
RN 70894-87-0 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(3-phenylpropyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



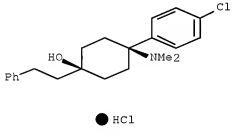
RN 70894-89-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



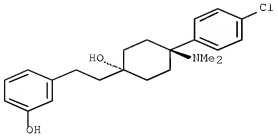
RN 70894-90-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



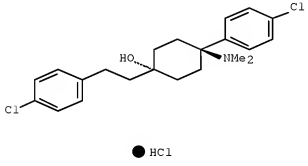
RN 70894-91-6 CAPLUS
CN Phenol, 3-[2-[4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxycyclohexyl]ethyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



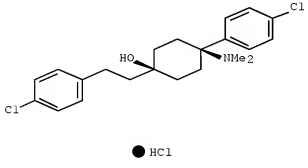
RN 70894-92-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethyl]-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



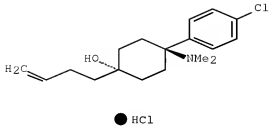
RN 70894-93-8 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethyl]-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



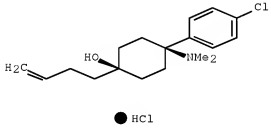
RN 70894-94-9 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



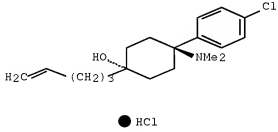
RN 70894-95-0 CAPLUS
CN Cyclohexanol, 1-(3-butenyl)-4-(4-chlorophenyl)-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



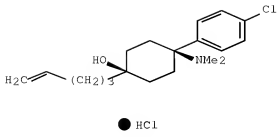
RN 70894-96-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



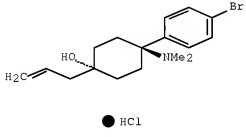
RN 70894-97-2 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(4-pentenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



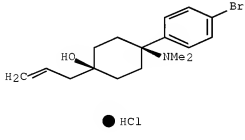
RN 70894-98-3 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



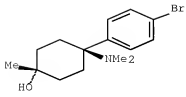
RN 70894-99-4 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-propenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



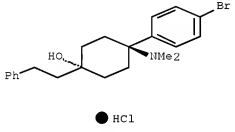
RN 70895-00-0 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.



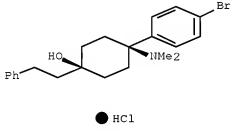
RN 70895-01-1 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



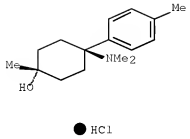
RN 70895-02-2 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-(2-phenylethyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



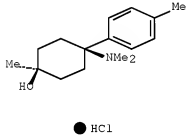
RN 70895-03-3 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-methyl-4-(4-methylphenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



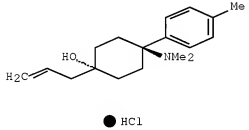
RN 70895-04-4 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-methyl-4-(4-methylphenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



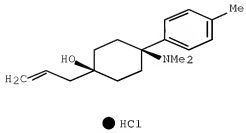
RN 70895-05-5 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-propenyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



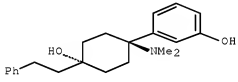
RN 70895-06-6 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-4-(4-methylphenyl)-1-(2-propenyl)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



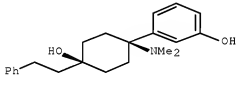
RN 70895-07-7 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(2-phenylethyl)cyclohexyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



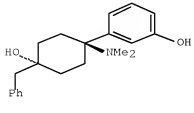
RN 70895-08-8 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(2-phenylethyl)cyclohexyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



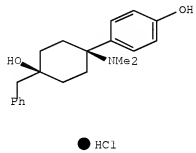
RN 70895-09-9 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-hydroxy-4-(phenylmethyl)cyclohexyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



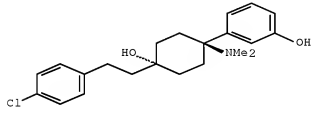
RN 70895-10-2 CAPLUS
CN Phenol, 4-[1-(dimethylamino)-4-hydroxy-4-(phenylmethyl)cyclohexyl]-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



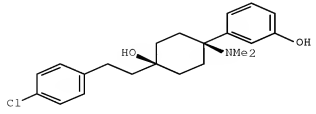
RN 70895-11-3 CAPLUS
CN Phenol, 3-[4-[2-(4-chlorophenyl)ethyl]-1-(dimethylamino)-4-hydroxycyclohexyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



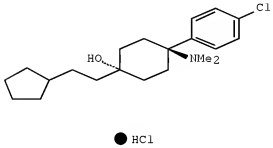
RN 70895-12-4 CAPLUS
CN Phenol, 3-[4-[2-(4-chlorophenyl)ethyl]-1-(dimethylamino)-4-hydroxycyclohexyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



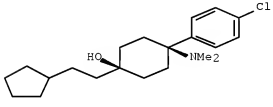
RN 70895-13-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclopentylethyl)-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



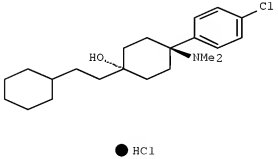
RN 70895-14-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclopentylethyl)-4-(dimethylamino)-, cis- (CA INDEX NAME)

Relative stereochemistry.



RN 70895-15-7 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclohexylethyl)-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

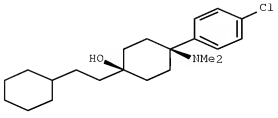
Relative stereochemistry.



RN 70895-16-8 CAPLUS

CN Cyclohexanol, 4-(4-chlorophenyl)-1-(2-cyclohexylethyl)-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

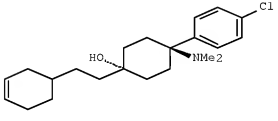
Relative stereochemistry.



● HCl

RN 70895-17-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(3-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

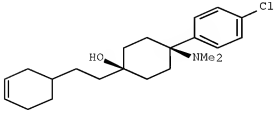
Relative stereochemistry.



● HCl

RN 70895-18-0 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(3-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

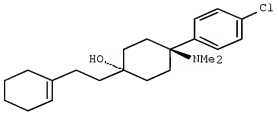
Relative stereochemistry.



● HCl

RN 70895-19-1 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(1-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

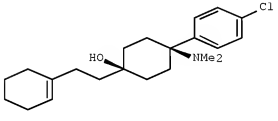
Relative stereochemistry.



● HCl

RN 70895-20-4 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-1-[2-(1-cyclohexen-1-yl)ethyl]-4-(dimethylamino)-, hydrochloride, cis- (9CI) (CA INDEX NAME)

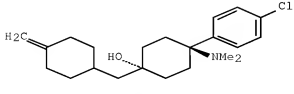
Relative stereochemistry.



● HCl

RN 70895-21-5 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-[(4-methylenecyclohexyl)methyl]-, hydrochloride, trans- (9CI) (CA INDEX NAME)

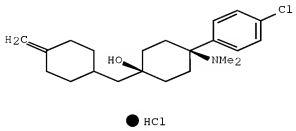
Relative stereochemistry.



● HCl

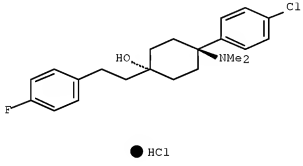
RN 70895-22-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-[(4-methylenecyclohexyl)methyl]-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



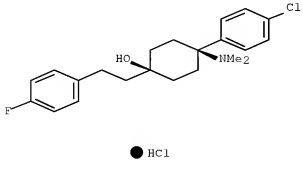
RN 70895-33-9 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



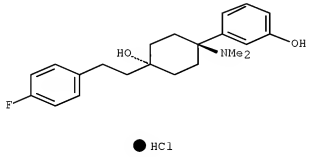
RN 70895-34-0 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



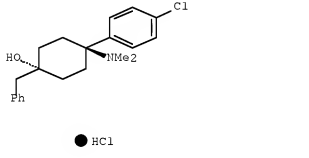
RN 70895-35-1 CAPLUS
CN Phenol, 3-[1-(dimethylamino)-4-[2-(4-fluorophenyl)ethyl]-4-hydroxycyclohexyl]-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



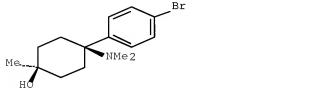
RN 70910-82-6 CAPLUS
CN Cyclohexanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-(phenylmethyl)-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 70936-62-8 CAPLUS
CN Cyclohexanol, 4-(4-bromophenyl)-4-(dimethylamino)-1-methyl-, cis- (CA INDEX NAME)

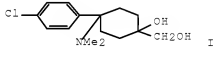
Relative stereochemistry.



L5 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:103511 CAPLUS Full-text
DOCUMENT NUMBER: 90:103511
ORIGINAL REFERENCE NO.: 90:16339a,16342a
TITLE: Compositions containing 4-amino-4-cyclohexan-1-ols
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4115589	A	19780919	US 1977-797782	19770517
US 4143156	A	19790306	US 1978-900673	19780427
PRIORITY APPLN. INFO.:			US 1977-797782 A3	19770517
OTHER SOURCE(S):	MARPAT 90:103511			

GI



I

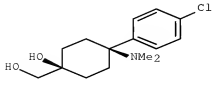
AB I, prepared from 4-hydroxycyclohexanone, is formulated into pharmaceutical compns. for the relief of pain in mammals. Thus, the ethylene monoketal of 1,4-cyclohexanedione is prepared in 91% yield from 4- hydroxycyclohexanone. Treatment of the monoketal with KCN and Me2NH.HCl gave a 78% yield of 4-cyano-4-dimethylaminocyclohexanone ethylene ketal which was treated with p-ClC6H4MgBr to give 4-(p-chlorophenyl)-4- dimethylaminocyclohexanone ethylene ketal hydrochloride in a 34% yield. The hydroxy protecting group of the latter compound is cleaved the product treated with a Wittig reagent, and the subsequent methylene compound oxidized to give I. Pharmaceutical compns. of I are described.

IT 69078-94-0P 69078-95-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and analgesic property of)

RN 69078-94-0 CAPLUS

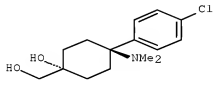
CN Cyclohexanemethanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxy-, cis- (CA INDEX NAME)

Relative stereochemistry.



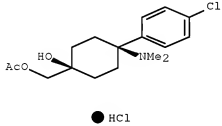
RN 69078-95-1 CAPLUS
CN Cyclohexanemethanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxy-, trans- (CA INDEX NAME)

Relative stereochemistry.



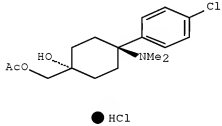
IT 69078-96-2P 69078-97-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 69078-96-2 CAPLUS
CN Cyclohexanemethanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxy-, α-acetate, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 69078-97-3 CAPLUS
CN Cyclohexanemethanol, 4-(4-chlorophenyl)-4-(dimethylamino)-1-hydroxy-, α-acetate, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



=> s l5 and (sundermann?/au or hennies?/au or koegel b?/au or wnendt?/au)

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            989 SUNDERMANN?/AU
            233 HENNIES?/AU
             48 KOEGEL B?/AU
             51 WNENDT?/AU
L19           3 L5 AND (SUNDERMANN?/AU OR HENNIES?/AU OR KOEGEL B?/AU OR WNENDT?
                /AU)

=> fil cap dissabs confsci wpix
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=> d que l18
L11          176 SEA ("SUNDERMANN B"/AU OR "SUNDERMANN BERND"/AU OR "SUNDERMANN
                 BERNHARD"/AU OR "SUNDERMANN BERNHARDT"/AU)
L12          136 SEA ("HENNIES H"/AU OR "HENNIES H "/AU OR "HENNIES H H"/AU OR
                 "HENNIES HAGEN H"/AU OR "HENNIES HAGEN HEINRICH"/AU)
L13           83 SEA ("KOEGEL B"/AU OR "KOEGEL B "/AU OR "KOEGEL B Y"/AU OR
                 "KOEGEL BABETTE"/AU OR "KOEGEL BABETTE YVONNE"/AU)
L14           68 SEA ("WNENDT S"/AU OR "WNENDT STEPHAN"/AU)
L15          354 SEA (L11 OR L12 OR L13 OR L14)
L18           59 SEA L15 AND (AMIN?(S) CYCLOHEX? OR AMINOCYCLOHEX?)


=> d sca ti l19

L19   3 ANSWERS   CAPLUS  COPYRIGHT 2008 ACS on STN
TI   Preparation of cyclohexylindoles as opioid receptor-like 1 (ORL1) receptor
     inhibitors

To display more answers, enter the number of answers you would like to
see.  To end the display, enter "NONE", "N", "0", or "END".
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L19   3 ANSWERS   CAPLUS  COPYRIGHT 2008 ACS on STN
TI   Preparation of substituted 4-aminocyclohexanols as regulators for the
     nociceptin/orphanin FQ ligand ORL-1 receptor system

L19   3 ANSWERS   CAPLUS  COPYRIGHT 2008 ACS on STN
TI   Preparation of 4-amino-4-(arylalkyl)cyclohexanols as ORL1 receptor ligands
     for treatment of pain

ALL ANSWERS HAVE BEEN SCANNED


=> s l20 not Preparation of cyclohexylindoles as opioid receptor?/ti
L21          49 L20 NOT PREPARATION OF CYCLOHEXYLINDOLES AS OPIOID RECEPTOR?/TI

=> s l21 not Preparation of substituted 4-aminocyclohexanols as regulators for the
nociceptin?/ti
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L26          48 L21 NOT PREPARATION OF SUBSTITUTED 4-AMINOCYCLOHEXANOLS AS REGUL
               ATORS FOR THE NOCICEPTIN?/TI

=> s l26 not as ORL1 receptor ligands?/ti
L28          47 L26 NOT AS ORL1 RECEPTOR LIGANDS?/TI

=> d  l28 ibib abs tot

L28  ANSWER 1 OF 47  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:99551  CAPLUS  Full-text
DOCUMENT NUMBER:          148:192112
TITLE:                    Preparation of spirocyclic azaindole derivatives with
                          affinity for opioid receptors
INVENTOR(S):              Zemolka, Saskia; Schunk, Stefan; Bergrath, Ellen;
                          Koegel, Babette-Yvonne; Englberger, Werner; Linz,
                          Klaus; Schick, Hans
PATENT ASSIGNEE(S):       Gruenenthal G.m.b.H., Germany
SOURCE:                   PCT Int. Appl., 91pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2008009416        A1    20080124    WO 2007-EP6326         20070717
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             GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
             KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG,
             MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
             RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR,
             TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
     DE 102006033114      A1    20080124    DE 2006-102006033114   20060718
PRIORITY APPLN. INFO.:                      DE 2006-102006033114A  20060718
OTHER SOURCE(S):          CASREACT 148:192112; MARPAT 148:192112
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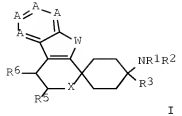

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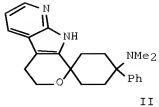

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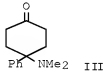
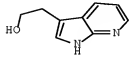


III



IV

AB The invention relates to substituted azaindole derivs. I [A = N, CR7-10, whereby at least one A is N and at most two A are N; W = NR4; X = NR17, O, S; R1, R2 = H, (un)branched, (un)saturated, (un)substituted C1-5-alkyl, C3-8-cycloalkyl, aryl-C1-3-alkyl, C3-8-cycloalkyl, heteroaryl; NR1R2 = CH2CH2OCH2CH2, CH2CH2NR10CH2CH2, (CH2)3-6; R3 = linear or branched, (un)substituted C1-8-alkyl, C3-8-cycloalkyl; aryl, heteroaryl, aryl-C1-3-alkyl, heteroaryl-C1-3-alkyl, cycloalkly-C1-3-alkyl; R4 = H, C1-5-alkyl, aryl, heteroaryl, COR12, SO2R12; R5 = :O, H, CO2R13, CONR13, OR13, C1-5-alkyl, C3-8-cycloalkyl, aryl, heteroaryl, etc.; R6 = H, F, Cl, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, CO2R13, NR14R15, C1-5-alkyl, etc.; R5R6 = (un)substituted (CH2)n; n = 2 - 6; R7, R8, R9, R10 = H, F, Cl, Br, I, NO2, CF3, OR13,SR13, SO2R13, SO2OR13, CN, CO2R13, NR14R15, C1-5-alkyl, C3-8-cycloalkyl, aryl, heteroaryl, etc; R12 = H, C1-5-alkyl, etc. R13 = H, C1-5-alkyl, C3-8-cycloalkyl, aryl, heteroaryl, etc.; R14, R15 = H, C1-5-alkyl, C3-8-cycloalkyl, aryl, heteroaryl, etc.; R14R15 = (CH2)2O(CH2)2, (CH2)2NR16(CH2)2, (CH2)3-6; R16 = H, C1-5-alkyl; R17 = H, C1-8-alkyl, COR12, SO2R12], their racemates, enantiomers, diastereomers, mixts., or physiol. acceptable salts, to methods for the production thereof, to medicaments containing said compds. and to the use of substituted azaindole derivs. for producing medicaments. Thus, 4-(dimethylamino)-4- phenylspiro[cyclohexan-1,8'-(5,6,8,9-tetrahydropyrano[3,4-b]-7-azaindole)] methanesulfonate [II·MeSO3H] was prepared from ketone III via cyclocondensation with indole IV. Ketone III was prepared from cyclohexane-1,4-dione monoethylene ketal, via amination/cyanation with aqueous Me2NH/KCN, then Grignard arylation with PhMgCl in THF and acid hydrolysis. Indole IV was prepared from 3-butyn-1-ol via disilylation with Et3SiCl in THF containing BuLi/hexane, chemoselective O-desilylation with HCl in MeOH, palladium-catalyzed cyclization with 3-iodopyridin-2-amine in DMF containing LiCl, Na2CO3 and catalytic [1,1'-bis(diphenylphosphino)ferrocene]pa lladium(II) chloride dichloromethane complex, and desilylation with Bu4NF in THF. The affinity for opioid receptors of II·MeSO3H was determined [Ki = 0.0053 μM vs. ORL1 receptor; Ki = 0.0044 μM vs. μ-opioid receptor; tail flick test: ED50 = 15 μg/kg (rat i.v.).].

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:788596 CAPLUS Full-text
DOCUMENT NUMBER: 147:188851
TITLE: Preparation of cyclohexylmethylamines as μ-opioid

receptor inhibitors
INVENTOR(S): Oberboersch, Stefan; Merla, Beatrix; Sundermann, Bernd; Englberger, Werner; Hennies, Hagen-Heinrich; Kless, Achim; Bloms-Funke, Petra; Koegel, Babette-Yvonne; Graubaum, Heinz
PATENT ASSIGNEE(S): Gruenenthal GmbH, Germany
SOURCE: PCT Int. Appl., 232pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007079930	A1	20070719	WO 2006-EP12224	20061219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
DE 102005061428	A1	20070816	DE 2005-102005061428	20051222

PRIORITY APPLN. INFO.: DE 2005-102005061428A 20051222
OTHER SOURCE(S): CASREACT 147:188851; MARPAT 147:188851
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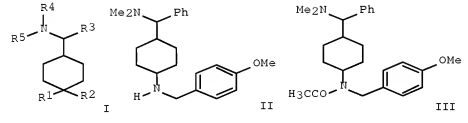


AB Title compds. I [R1 = alkyl, aryl, heteroaryl, etc.; R2 = H, OH with provisos; R3 = aryl, heteroaryl; R4, R5 = H, alkyl with provisos] and their pharmaceutically acceptable salts and formulations were prepared For example, N-acylation of amine II with acetyl chloride afforded cyclohexylmethylamine III. In μ-opioid receptor inhibition assays, 295-examples of compds. I exhibited 71->100 % inhibition at 1μM.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1283424 CAPLUS Full-text
DOCUMENT NUMBER: 146:45499

TITLE: Substituted N-acylbenzo[d]isoxazol-3-amine ligands for mGluR5, serotonin-(5-HT) and noradrenaline receptors as analgesics for prophylaxis or treatment of acute, chronic, visceral or neuropathic pain

INVENTOR(S): Merla, Beatrix; Gerlach, Matthias; Sundermann, Corinna; Jagusch, Utz-Peter; Hennies, Hagen-Heinrich; Oberboersch, Stefan; Haurand, Michael; Jostock, Ruth; Reich, Melanie

PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany

SOURCE: Ger. Offen., 72pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102005026194	A1	20061207	DE 2005-102005026194	20050606
CA 2610373	A1	20061214	CA 2006-2610373	20060606
WO 2006131296	A1	20061214	WO 2006-EP5356	20060606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1893589	A1	20080305	EP 2006-761974	20060606
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: DE 2005-102005026194A 20050606
WO 2006-EP5356 W 20060606

OTHER SOURCE(S): MARPAT 146:45499

AB The title compds., N-(R5CO)-7-R1-6-R2-5-R3-4-R4-benzo[d]isoxazol-3-amines [1, R1-R4 = H, halo, CN, NC, NO2, SO3H, SO2NH2, (alkyl)amino, OH, SH, C1-10 alkyl, alkoxy, aralkoxy, alkylthio, aralkylthio, acylamino, carboxamide, acyl, carboxy, ester; R5 = C1-10 alkyl, C2-10 alkenyl, 3-9-membered (poly)cycloalkyl, imidazolidinonyl, (hetero)aryl, ω-alkoxycarbonylalkyl; preferably R1 = H, halo; R2 = H, halo, NH2, R3, R4 = H, halo, NH2, Me, Et, nPr, iPr, Bu, iBu, tBu, alkoxy, aralkoxy, dialkylamino; R5 = C1-9 (un)branched optionally fluorinated alkyl, C3-7 cycloalkyl, bicyclo[3.1.1]heptyl, adamantyl, substituted Ph, naphthyl, hetaryl] useful as inhibitors for metabotropic glutamate 5 receptors (mGluR5), noradrenaline and serotonin receptors for treatment of disorders and diseases controlled by these receptors, such as chronic and acute pain, nutrition disorders, behavior disorders, neurodegenerative diseases, abuses, cough, asthma, glaucoma, and for local anesthesia in various types of formulations (no trial data), were prepared by a process comprising cyclocondensation of 2-fluoro-3-R1-4-R2-5-R3-6-R4-benzonitriles (3) with N-acetylhydroxylamine followed by acylation of the intermediate 7-R1-6-R2-5-R3-4-R4-benzo[d]isoxazol-3-amines (2, same R1-R4) by carboxylic acids or acyl chlorides R5COX (same R5, X = Cl, OH) in the presence of a coupling reagent or a base, resp. In an example, 4-(4-methylphenylmethoxy)benzo[d]oxazol-3-amine (2-2) was prepared by cyclocondensation of 1.1 equiv of N-acetylhydroxylamine with 2-fluoro-6-(4-

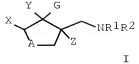
methylphenylmethoxy)benzonitrile and 1.1 equiv of KOtBu in 1.45 mL/mol of DMF at 50° for 1 h; acylation of 2-2 by an automated procedure by 5 equiv of 3-NO2C6H4COCl in the presence of 1 equiv of Et3N in pyridine gave the target compound, N-[4-(methylphenylmethoxy)benzo[d]isoxazol-3-yl]-3-nitrobenzamide (1-167). In another example, the compound 1-167 exhibited 39.74% of inhibition of glutamate uptake by rat brain mGluR5 receptors in concentration of 10μM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:525971 CAPLUS Full-text
DOCUMENT NUMBER: 141:89012
TITLE: Preparation of saturated and unsaturated heteroaryl cycloalkyl methylamines as antidepressants or analgesics
INVENTOR(S): Bloms-Funke, Petra; Englberger, Werner; Graudums, Ivars; Griebel, Carsten; Hennies, Hagen-Heinrich; Kaulartz, Dagmar; Kless, Achim; Puetz, Claudia; Reinardy, Sabine; Saunders, Derek; Schiene, Klaus; Sundermann, Bernd; Zimmer, Oswald
PATENT ASSIGNEE(S): Gruenenthal GmbH, Germany
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10261091	A1	20040701	DE 2002-10261091	20021220
CA 2509072	A1	20040729	CA 2003-2509072	20031219
WO 2004063161	A1	20040729	WO 2003-EP14653	20031219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003296693	A1	20040810	AU 2003-296693	20031219
EP 1572653	A1	20050914	EP 2003-815065	20031219
EP 1572653	B1	20071121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006523182	T	20061012	JP 2004-566009	20031219
US 2006025456	A1	20060202	US 2005-155766	20050620
PRIORITY APPLN. INFO.:			DE 2002-10261091 A	20021220
			WO 2003-EP14653 W	20031219

OTHER SOURCE(S): MARPAT 141:89012
GI



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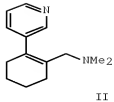


II

AB The present invention concerns saturated and unsatd. heteroaryl cycloalkyl methylamines I [R1, R2 = H, (un)substituted, (un)branched C1-10-alkyl, C2-10-alkenyl, C3-10-alkynyl, (un)substituted, (un)saturated C3-7-cycloalkyl, heterocycle containing S, O, NR3; R1R2 = (un)substituted, (un)saturated C3-7-cycloalkyl, heterocycle (optionally containing O, S, NR4); R3 = H, (un)substituted, (un)branched C1-10-alkyl, C2-10-alkenyl, C3-10-alkynyl, (un)substituted, (un)saturated alkylaryl, (un)substituted aryl; R4 = H, (un)substituted, (un)branched C1-10-alkyl, C2-10-alkenyl, C3-10-alkynyl; A = (CH2)n; n = 1 - 4; G = 5- or 6-membered aromatic (containing 1 or 2 N), ; when Y = H, OH, Cl, then X = Z = H; when XY = bond, then Z = H; when YZ = bond, then X = H], their racemates, enantiomers, diastereomers, and esp, a mixture of their enantiomers or diastereomers, as free bases and as their physiol. acceptable salts, especially HCl salts, procedures for their production, drug, containing these compds., as well as the use of these compds. to the production of drugs as well as procedure for the treatment of depressions and/or pain. Thus, dimethyl[{2-(pyridin-3-yl)cyclohexen-1-yl}methyl]amine (II) was prepared from 3-bromopyridine in Et2O via lithiation with BuLi in hexane, reaction with 2-[(dimethylamino)methyl]cyclohexanone, chlorination with SOCl2, and dehydrochlorination with aqueous NaOH. The pharmacol. of II was determined [83% inhibition of 5-HT receptor and 35% inhibition of nicotinic-acetylcholine receptor (each at 10 μM); ED50 = 1.66 mg/kg (i.v.) in formalin test of mouse (analgesic activity); 54% shortening of immobility phase at 21.5 mg/kg (i.p.) in forced swimming test of mouse (antidepressant activity)].
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:428890 CAPLUS Full-text
DOCUMENT NUMBER: 141:6856
TITLE: Preparation of 4-alkyl-1-aryl-cyclohexylamines as ORL-1 receptor ligands for the treatment of pain.
INVENTOR(S): Sundermann, Bernd; Schick, Hans
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

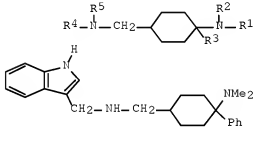
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043899	A1	20040527	WO 2003-EP12313	20031105

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10252665	A1	20040603	DE 2002-10252665		20021111
AU 2003301968	A1	20040603	AU 2003-301968		20031105
EP 1562891	A1	20050817	EP 2003-810965		20031105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005245593	A1	20051103	US 2005-125359		20050510
US 7173045	B2	20070206			
PRIORITY APPLN. INFO.:			DE 2002-10252665	A	20021111
			WO 2003-EP12313	W	20031105

OTHER SOURCE(S): MARPAT 141:6856
GI



I

II

AB Title compds. I [R1, R2 = H, alkyl, cycloalkyl, etc.; R3 = alkyl, cycloalkyl, (un)substituted aryl, etc.; R4 = H, (un)substituted alkyl; R5 = H, (un)substituted cycloalkyl, aryl, etc.] and their pharmaceutically acceptable salts were prepared For example, sodium triacetoxyborohydride mediated reductive amination (1H-indol-3-yl)methylamine and 4-dimethylamino-4-phenylcyclohexan-1-aldehyde afforded the claimed nonpolar diastereomer of cyclohexylamine II. In ORL-1 receptor binding assays, 42-examples of compds. I exhibited Ki values ranging from 1.2-92 nM, the Ki of cyclohexylamine II was 210 nM. Compds. I are claimed useful for the treatment of acute, visceral and chronic pain.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2003:777742 CAPLUS Full-text
DOCUMENT NUMBER:	139:291992
TITLE:	Preparation of substituted 4-aminocyclohexanols for treatment of pain
INVENTOR(S):	Sundermann, Bernd; Hennies, Hagen-Heinrich; Englberger, Werner; Koegel, Babette-Yvonne
PATENT ASSIGNEE(S):	Gruenenthal G.m.b.H., Germany
SOURCE:	PCT Int. Appl., 124 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080557	A1	20031002	WO 2003-EP2812	20030318
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10213051	A1	20031030	DE 2002-10213051	20020323
CA 2480038	A1	20031002	CA 2003-2480038	20030318
AU 2003212366	A1	20031008	AU 2003-212366	20030318
EP 1487778	A1	20041222	EP 2003-708253	20030318
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005526795	T	20050908	JP 2003-578315	20030318
US 2005187220	A1	20050825	US 2004-947551	20040923
US 7211694	B2	20070501		

PRIORITY APPLN. INFO.: DE 2002-10213051 A 20020323
WO 2003-EP2812 W 20030318

OTHER SOURCE(S): CASREACT 139:291992; MARPAT 139:291992

GI

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AB Aminocyclohexanols I [R1, R2 = H, (un)substituted aliphatic, cycloalkyl, aryl, heterocyclyl; R1R2 = CH2CH2OCH2CH2, (un)substituted CH2CH2NHCH2CH2, (CH2)3-6; R3 = (un)substituted aliphatic, cycloalkyl, aryl, heterocyclyl; R4 = (un)substituted cycloalkyl, aryl, heterocyclyl] were prepared Thus, 1,4-dioxaspiro[4.5]decan-8-one was reduced to the alc., o-benzylated, hydrolyzed to the ketone, and treated with Me2NH>HCl and KCN to give 4-benzyloxy-1-dimethylaminocyclohexanecarbonitrile which was treated with PhMgBr and NH4Cl to give I [R1, R2 = Me, R3 = Ph, R4 = PhCH2] whose diastereomers were separated The diastereomers had IC50 for ORL-1 binding of 0.069 and 0.40 μM, resp.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:356431 CAPLUS Full-text
DOCUMENT NUMBER: 138:368915
TITLE: Preparation of 2(1H)-quinoxalinones as analgesics
INVENTOR(S): Sattlegger, Michael; Buschmann, Helmut; Przewosny, Michael; Enlgberger, Werner; Koegel, Babette-Yvonne;

	Schick, Hans
PATENT ASSIGNEE(S):	Gruenenthal G.m.b.H., Germany
SOURCE:	PCT Int. Appl., 89 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037879	A1	20030508	WO 2002-EP11832	20021023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10153345	A1	20030508	DE 2001-10153345	20011029
CA 2465061	A1	20030508	CA 2002-2465061	20021023
AU 2002350608	A1	20030512	AU 2002-350608	20021023
EP 1444212	A1	20040811	EP 2002-785285	20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 2004001829	A2	20050128	HU 2004-1829	20021023
HU 2004001829	A3	20050628		
JP 2005512986	T	20050512	JP 2003-540161	20021023
US 2004224954	A1	20041111	US 2004-832205	20040426
PRIORITY APPLN. INFO.:			DE 2001-10153345 A	20011029
			WO 2002-EP11832 W	20021023
OTHER SOURCE(S):	MARPAT 138:368915			

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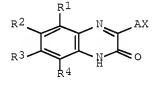


I

AB Title compds. [I; R1-R4 = H, halo, OH, (branched) (saturated) C1-10 aliphatic group, C3-7 cycloaliph. group; whereby the both aliphatic and cycloaliph. groups are bonded by an ether bridge; A = (CH2)n+2, (CH2)nCH:CH, (CH2)nCO2, (CH2)nCONH, (CH2)n+1O(CH2)pCO, (CH2)n+1O, (CH2)n+1NR8, NH(CH2)r; p = 0, 1; n = 0-3; r = 0-2; R8 = H, (branched) (saturated) C1-10 aliphatic group, C3-7 cycloaliph. group, (hetero)aryl; X = (substituted) phenylcyclohexyl, etc.], were prepared Thus, 6,7-dimethyl-3-oxo-3,4- dihydroquinoxaline-2-carboxylic acid (preparation given) was reacted with 4-amino-2-(N,N-dimethylaminomethyl)-1-(3-methoxyphenyl)cyclohexan-1-ol in the presence of N-methylmorpholine, dicyclohexylcarbodiimide, and hydroxybenzotriazole in DMF to give 69% (6,7-

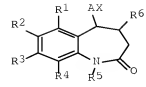
dimethyl-3-oxo-3,4- dihydroquinoxalin-2-yl)-N-[3-(N,N-dimethylaminomethyl)-4-hydroxy-4-(3- methoxyphenyl)cyclohexyl]carboxamide. The latter at 10 mg/kg i.v. in mice gave 72% inhibition of phenylquinone-induced writhing.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:356425 CAPLUS Full-text
DOCUMENT NUMBER: 138:353845
TITLE: Preparation of 2H-1-benzazepin-2-ones as analgesics
INVENTOR(S): Sattlegger, Michael; Buschmann, Helmut; Przewosny, Michael; Englberger, Werner; Koegel, Babette-Yvonne; Schick, Hans
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037873	A1	20030508	WO 2002-EP11830	20021023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10153348	A1	20030508	DE 2001-10153348	20011029
CA 2464191	A1	20030508	CA 2002-2464191	20021023
AU 2002349002	A1	20030512	AU 2002-349002	20021023
EP 1444206	A1	20040811	EP 2002-781280	20021023
EP 1444206	B1	20060315		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 2004001762	A2	20041228	HU 2004-1762	20021023
JP 2005511570	T	20050428	JP 2003-540155	20021023
AT 320418	T	20060415	AT 2002-781280	20021023
PT 1444206	T	20060731	PT 2002-781280	20021023
ES 2260487	T3	20061101	ES 2002-781280	20021023
US 2004224938	A1	20041111	US 2004-824244	20040414
US 7041662	B2	20060509		
PRIORITY APPLN. INFO.:			DE 2001-10153348 A	20011029
			WO 2002-EP11830 W	20021023

OTHER SOURCE(S): MARPAT 138:353845
GI



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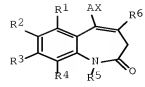


II

AB Title compds. [I; R1-R4 = H, halo, OH, (branched) (saturated) C1-10 aliphatic group, C3-7 cycloaliph. group; whereby the both aliphatic and cycloaliph. groups are bonded by an ether bridge; R5 = H, (branched) (saturated) C1-10 aliphatic group, (hetero)aryl; R6 = OH, CH2NR72; R7 = (branched) (saturated) C1-6 aliphatic group, C3-6 cycloaliph. group; or NR7 = 3-8 membered cyclyl; A = (CH2)n+2, (CH2)nCH:CH, (CH2)nCO2, (CH2)nCONH, (CH2)n+1O(CH2)pCO, (CH2)n+1O, (CH2)n+1NR8; p = 0, 1; n = 0-3; R8 = H, (branched) (saturated) C1-10 aliphatic group, C3-7 cycloaliph. group, (hetero)aryl; X = (substituted) phenylcyclohexyl, etc.], were prepared Thus, 4-amino-2-(N,N-dimethylaminomethyl)-1-(3-methoxyphenyl)cyclohexan-1-ol was reacted with (8-chloro-1-methyl-2-oxo-2,3-dihydro-1H-1-benzazepin-5- yl)acetic acid (analog preparation given) in the presence of dicyclohexylcarbodiimide, N-methylmorpholine, and 1-hydroxybenzotriazole in DMF to give 75% (8-chloro-1-methyl-2-oxo-2,3-dihydro-1H-1-benzazepin-5- yl)-N-[3-(N,N-dimethylaminomethyl)-4-hydroxy-4-(3- methoxyphenyl)cyclohexyl]acetamide. The latter at 10 mg/kg i.v. in mice gave 25% inhibition of phenylquinone-induced writhing.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

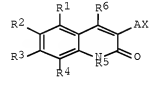
L28 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:356422 CAPLUS Full-text
DOCUMENT NUMBER: 138:353843
TITLE: Preparation of 2(1H)-quinolinones as analgesics
INVENTOR(S): Sattlegger, Michael; Buschmann, Helmut; Przewosny, Michael; Englberger, Werner; Koegel, Babette-Yvonne; Schick, Hans
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037870	A1	20030508	WO 2002-EP11833	20021023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

DE 10153347	A1	20030508	DE 2001-10153347		20011029
CA 2465306	A1	20030508	CA 2002-2465306		20021023
AU 2002346861	A1	20030512	AU 2002-346861		20021023
EP 1442021	A1	20040804	EP 2002-782979		20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
HU 2004001831	A2	20041228	HU 2004-1831		20021023
JP 2005511567	T	20050428	JP 2003-540152		20021023
US 2004224980	A1	20041111	US 2004-832191		20040426
MX 2004PA04090	A	20040708	MX 2004-PA4090		20040429
PRIORITY APPLN. INFO.:			DE 2001-10153347	A	20011029
			WO 2002-EP11833	W	20021023

OTHER SOURCE(S): MARPAT 138:353843

GI



I

AB Title compds. [I; R1-R4 = H, halo, OH, (branched) (saturated) C1-10 aliphatic group, C3-7 cycloaliph. group; whereby the both aliphatic and cycloaliph. groups are bonded by an ether bridge; R5 = H, (branched) (saturated) C1-10 aliphatic group, (hetero)aryl; R6 = OH, OR7; R7 = (branched) (saturated) C1-10 aliphatic group, C3-6 cycloaliph. group; A = (CH2)3, CH2CH:CH, CH2CO2, CH2CONH, (CH2)2O(CH2)pCO, (CH2)2O, (CH2)2NR8; p = 0, 1; R8 = H, (branched) (saturated) C1-10 aliphatic group, C3-7 cycloaliph. group, (hetero)aryl; X = (substituted) phenylcyclohexyl, etc.], were prepared Thus, (7-chloro-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)acetic acid (preparation given) was reacted with 4-amino-2-(N,N-dimethylaminomethyl)-1-(3-methoxyphenyl)cyclohexan-1-ol in the presence of N-methylmorpholine, dicyclohexylcarbodiimide, and hydroxybenzotriazole in DMF to 2-(7-chloro-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[3-(N,N- dimethylaminomethyl)-4-hydroxy-4-(3-methoxyphenyl)cyclohexyl]acetamide with a yield of 48%. The latter at 10 mg/kg i.v. in mice gave 60% inhibition of phenylquinone-induced writhing.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN

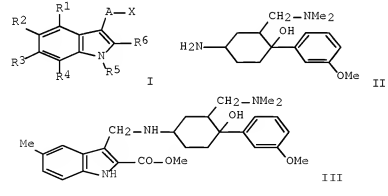
ACCESSION NUMBER:	2003:356417 CAPLUS Full-text
DOCUMENT NUMBER:	138:368760
TITLE:	Preparation of 1H-indole-2-carboxylic acids and related compounds for the treatment of pain
INVENTOR(S):	Sattlegger, Michael; Buschmann, Helmut; Przewosny, Michael; Enlgberger, Werner; Koegel, Babette-Yvonne; Schick, Hans
PATENT ASSIGNEE(S):	Gruenenthal G.m.b.H., Germany
SOURCE:	PCT Int. Appl., 100 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037863	A2	20030508	WO 2002-EP11831	20021023
WO 2003037863	A3	20040812		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10153346	A1	20040422	DE 2001-10153346	20011029
CA 2465236	A1	20030508	CA 2002-2465236	20021023
AU 2002349003	A1	20030512	AU 2002-349003	20021023
EP 1472221	A2	20041103	EP 2002-781281	20021023
EP 1472221	B1	20060322		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 2004002076	A2	20050228	HU 2004-2076	20021023
JP 2005511566	T	20050428	JP 2003-540145	20021023
AT 321026	T	20060415	AT 2002-781281	20021023
PT 1472221	T	20060831	PT 2002-781281	20021023
ES 2261748	T3	20061116	ES 2002-781281	20021023
US 2004225003	A1	20041111	US 2004-831937	20040426
US 7217729	B2	20070515		

PRIORITY APPLN. INFO.: DE 2001-10153346 A 20011029
WO 2002-EP11831 W 20021023

OTHER SOURCE(S): CASREACT 138:368760; MARPAT 138:368760
GI



AB Title compds. I [R1, R2, R3, R4 = (un)substituted alkyl, cycloalkyl; R5 = H, (un)substituted alkyl, cycloalkyl, etc.; R6 = OH, halo, CN, etc.; A = -(CH2)nCOO-, -(CH2)nCONH-, -(CH2)nO-; n = 0-3; X = (un)substituted piperidin-1-

yl, cyclohexyl, dihydro-1H-isoquinolin-2-yl, etc.] and their pharmaceutically acceptable salts were prepared For example, reductive amination condensation of cyclohexylamine II and 5-methyl-3-formyl-1H- indol-2-carboxylic acid Me ester afforded indole III in 82% yield. In phenylquinone-induced writhing studies with mice, 4-examples of I exhibited 48-100% inhibition at 10 mg/kg i.v. dosage, e.g., indole III displayed 48% inhibition. Compds. I provided medium-strong to strong analgesic effects.

L28 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:868898 CAPLUS Full-text
DOCUMENT NUMBER: 137:369762
TITLE: Preparation of cyclohexane-1,4-diamines as regulators of the ORL1 opioid receptor
INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-Heinrich; Englberger, Werner; Koegel, Babette-Yvonne
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 256 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090317	A1	20021114	WO 2002-EP5051	20020508
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10123163	A1	20030116	DE 2001-10123163	20010509
CA 2446461	A1	20021114	CA 2002-2446461	20020508
AU 2002312883	A1	20021118	AU 2002-312883	20020508
AU 2002312883	B2	20070906		
EP 1392641	A1	20040303	EP 2002-738038	20020508
EP 1392641	B1	20070411		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009580	A	20040622	BR 2002-9580	20020508
HU 2004000888	A2	20040728	HU 2004-888	20020508
CN 1533374	A	20040929	CN 2002-813753	20020508
CN 1537100	A	20041013	CN 2002-813557	20020508
JP 2004533439	T	20041104	JP 2002-587399	20020508
NZ 529147	A	20061027	NZ 2002-529147	20020508
AT 359260	T	20070515	AT 2002-738038	20020508
AT 370120	T	20070915	AT 2002-750900	20020508
ES 2284876	T3	20071116	ES 2002-738038	20020508
ES 2291486	T3	20080301	ES 2002-750900	20020508
NO 2003004930	A	20040105	NO 2003-4930	20031105
MX 2003PA10134	A	20040310	MX 2003-PA10134	20031106
US 2004162287	A1	20040819	US 2003-704329	20031110
US 7276518	B2	20071002		
ZA 2003009521	A	20040928	ZA 2003-9521	20031208
ZA 2003009522	A	20041202	ZA 2003-9522	20031208

PRIORITY APPLN. INFO.: DE 2001-10123163 A 20010509
WO 2002-EP5051 W 20020508

OTHER SOURCE(S): MARPAT 137:369762

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II

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AB Title compds. I [R1, R2 = H, alkyl, cycloalkyl, etc. or R1 and R2 together form a ring, e.g., CH2CH2OCH2CH2,(CH2)3-6, CH2CH2NR6CH2CH2; R6 = H, alkyl, cycloalkyl, etc.; R3 = alkyl, cycloalkyl, (un)substituted aryl, etc.; R4 = H, alkyl, C(X)R7; X = O, S; R7 = H, alkyl, cycloalkyl, etc.; R5 = cycloalkyl, aryl, heteroaryl, etc.] and their pharmaceutically acceptable salts were prepared For example, reductive amination of ketone II, e.g., prepared from 1,4-dioxaspiro[4.5]decan-8-one in 3-steps, and benzylamine afforded after chromatog., the nonpolar diastereomer of diamine III.HCL. In ORL1 opioid receptor binding assays, 91-specific examples of compds. I exhibited binding to the receptor with Ki values ranging from 0.0004-0.75 μM, e.g., the Ki of the nonpolar diastereomer of diamine III.HCL = 0.010 μM. Compds. I may be useful in the treatment of anxiety, depression, epilepsy, etc.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:868721 CAPLUS Full-text
DOCUMENT NUMBER: 137:369761
TITLE: Preparation of cyclohexane-1,4-diamines as regulators of the μ-opioid receptor
INVENTOR(S): Friderichs, Elmar Josef; Sundermann, Bernd; Hinze, Claudia; Koegel, Babette-Yvonne
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002089783	A1	20021114	WO 2002-EP5122	20020509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10123163	A1	20030116	DE 2001-10123163		20010509
CN 1533374	A	20040929	CN 2002-813753		20020508
CN 1537100	A	20041013	CN 2002-813557		20020508
AT 359260	T	20070515	AT 2002-738038		20020508
AT 370120	T	20070915	AT 2002-750900		20020508
ES 2284876	T3	20071116	ES 2002-738038		20020508
ES 2291486	T3	20080301	ES 2002-750900		20020508
CA 2446735	A1	20021114	CA 2002-2446735		20020509
AU 2002341210	A1	20021118	AU 2002-341210		20020509
EP 1385493	A1	20040204	EP 2002-769145		20020509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 2004000963	A2	20040830	HU 2004-963		20020509
JP 2005515959	T	20050602	JP 2002-586920		20020509
MX 2003PA10195	A	20040310	MX 2003-PA10195		20031107
US 2004229872	A1	20041118	US 2003-704524		20031110
ZA 2003009521	A	20040928	ZA 2003-9521		20031208
ZA 2003009522	A	20041202	ZA 2003-9522		20031208

PRIORITY APPLN. INFO.: DE 2001-10123163 A 20010509
WO 2002-EP5122 W 20020509

OTHER SOURCE(S): MARPAT 137:369761

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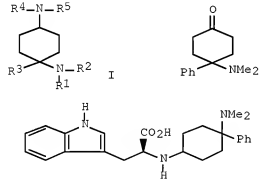


AB Title compds. I [R1, R2 = H, alkyl, cycloalkyl, etc. or R1 and R2 together form a ring, e.g., CH2CH2OCH2CH2,(CH2)3-6, CH2CH2NR6CH2CH2; R6 = H, alkyl, cycloalkyl, etc.; R3 = alkyl, cycloalkyl, (un)substituted aryl, etc.; R4 = H, alkyl, C(X)R7; X = O, S; R7 = H, alkyl, cycloalkyl, etc.; R5 = cycloalkyl, aryl, heteroaryl, etc.] and their pharmaceutically acceptable salts were prepared For example, reductive amination of ketone II, e.g., prepared from 1,4-dioxaspiro[4.5]decan-8-one in 3-steps, and L-tryptophan Me ester hydrochloride, followed by ester hydrolysis, afforded after chromatog. and

workup the calcium salt of the nonpolar diastereomer of diamine III. In μ-opioid receptor binding assays, 9-specific examples of compds. I exhibited binding to the receptor with Ki values ranging from 0.0008-0.140 μM, e.g., the Ki of the calcium salt of the nonpolar diastereomer of diamine III = 0.0011 μM. Compds. I may be useful in the treatment of irritable bowel syndrome, diarrhea, peripheral pain, etc.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:293594 CAPLUS Full-text
DOCUMENT NUMBER: 136:309753
TITLE: Preparation of 5-amino-1-penten-3-ols as analgesics
INVENTOR(S): Buschmann, Helmut; Maul, Corinna; Sundermann, Bernd; Jagusch, Utz-Peter; Haurand, Michael; Chizh, Boris
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030869	A1	20020418	WO 2001-EP11244	20010928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10048714	A1	20020411	DE 2000-10048714	20000930
AU 2002021632	A	20020422	AU 2002-21632	20010928
CA 2424103	A1	20030328	CA 2001-2424103	20010928
EP 1322590	A1	20030702	EP 2001-986671	20010928
EP 1322590	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014459	A	20030923	BR 2001-14459	20010928
HU 2003003110	A2	20040301	HU 2003-3110	20010928
HU 2003003110	A3	20060228		
JP 2004511458	T	20040415	JP 2002-534258	20010928
CN 1649826	A	20050803	CN 2001-816492	20010928
NZ 525417	A	20051125	NZ 2001-525417	20010928
RU 2289571	C2	20061220	RU 2003-111758	20010928
AT 361274	T	20070515	AT 2001-986671	20010928
ES 2286154	T3	20071201	ES 2001-986671	20010928
NO 2003001388	A	20030522	NO 2003-1388	20030326
MX 2003PA02734	A	20030728	MX 2003-PA2734	20030328
US 2003220390	A1	20031127	US 2003-402259	20030331
US 6815443	B2	20041109		
ZA 2003003301	A	20040812	ZA 2003-3301	20030429

PRIORITY APPLN. INFO.:			
DE 2000-10048714	A	20000930	
DE 2000-10048715	A	20000930	
WO 2001-EP11244	W	20010928	

OTHER SOURCE(S): MARPAT 136:309753
AB Title compds. R6CH:CR1CR5(OH)CHR2CHR7NR3R4 [I; R1,R2 = (un)substituted alk(en)yl, etc.; R1R2 = (un)substituted alkylene; R3,R4 = alkyl, Ph, CH2Ph, etc.; NR3R4 = heterocyclyl; R5 = alkyl, (hetero)aryl(alkyl), etc.; R6 = alkyl, (hetero)aryl, etc.; R7 = H or (hetero)aryl] were prepared Data for biol. activity of I were given.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:275949 CAPLUS Full-text
DOCUMENT NUMBER: 136:309754
TITLE: Preparation of (arylmethylidene)(aminomethyl)cycloalkanols as analgesics.
INVENTOR(S): Buschmann, Helmut; Maul, Corinna; Sundermann, Bernd; Jagusch, Utz-Peter; Haurand, Michael; Chizh, Boris
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028816	A1	20020411	WO 2001-EP10881	20010920
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10048714	A1	20020411	DE 2000-10048714	20000930
AU 2002012263	A	20020415	AU 2002-12263	20010920
CN 1649826	A	20050803	CN 2001-816492	20010928
AT 361274	T	20070515	AT 2001-986671	20010928
ES 2286154	T3	20071201	ES 2001-986671	20010928
ZA 2003003301	A	20040812	ZA 2003-3301	20030429
PRIORITY APPLN. INFO.:			DE 2000-10048714 A	20000930
			WO 2001-EP10881 W	20010920

OTHER SOURCE(S): MARPAT 136:309754
AB R6CH:CR1C(OH)R5CHR2CHR7NR3R4 [R1, R2 = (substituted) (unsatd.) alkyl; R1R2 = atoms to form a (substituted) (unsatd.) (CH2)2-9 ring; R3, R4 = (substituted) (unsatd.) alkyl, cycloalkyl, Ph, PhCH2, PhCH2CH2; R3R4 = (CH2)3-6, CH2CH2OCH2CH2; R5 = (substituted) (unsatd.) alkyl, cycloalkyl, aryl, heteroaryl, aralkyl, cycloalkylalkyl, heteroarylalkyl; R6 = (substituted) (unsatd.) alkyl, cycloalkyl, aryl, heteroaryl; R7 = H, (substituted) aryl, heteroaryl], are claimed (none are synthesized). Several title compds. at 2.5-10 mg/kg i.v. reduced phenylquinone-induced writhing in mice.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

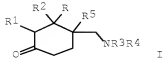
L28 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:507665 CAPLUS Full-text
DOCUMENT NUMBER: 135:92444
TITLE: Preparation of aminomethylphenylcyclohexanones as

analgesics
INVENTOR(S): Puetz, Claudia; Buschmann, Helmut; Koegel, Babette-Yvonne
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049651	A2	20010712	WO 2000-EP13282	20001227
WO 2001049651	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10000311	A1	20010712	DE 2000-10000311	20000105
CA 2396310	A1	20010712	CA 2000-2396310	20001227
EP 1246791	A2	20021009	EP 2000-990824	20001227
EP 1246791	B1	20041027		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000016941	A	20030225	BR 2000-16941	20001227
HU 2002003859	A2	20030328	HU 2002-3859	20001227
HU 2002003859	A3	20080128		
JP 2003519209	T	20030617	JP 2001-550191	20001227
NZ 520468	A	20031128	NZ 2000-520468	20001227
AT 280752	T	20041115	AT 2000-990824	20001227
PT 1246791	T	20050331	PT 2000-990824	20001227
ES 2231304	T3	20050516	ES 2000-990824	20001227
AU 782862	B2	20050901	AU 2001-30169	20001227
NO 2002002983	A	20020828	NO 2002-2983	20020620
KR 748378	B1	20070810	KR 2002-708706	20020704
MX 2002PA06697	A	20020930	MX 2002-PA6697	20020705
US 2003096811	A1	20030522	US 2002-189184	20020705
US 6890959	B2	20050510		
ZA 2002006150	A	20031103	ZA 2002-6150	20020801
HK 1050890	A1	20050527	HK 2003-102442	20030404

PRIORITY APPLN. INFO.: DE 2000-10000311 A 20000105
WO 2000-EP13282 W 20001227

OTHER SOURCE(S): MARPAT 135:92444
GI



I

AB Title compds. [I; R = H, halo, OH, alkoxy, alkanoyloxy, etc.; R1 = R5 = H; RR1,RR5 = bond; R2 = (un)substituted Ph; R3,R4 = H, alkyl, (hetero)aryl, etc.; NR3R4 = heterocyclyl] were prepared Thus, 1,3-cyclohexanedione was condensed with Me2C(CH2OH)2 and the product aminomethylated by Me2N:CH2Cl to give 9-dimethylamino-1,5-dioxaspiro[5.5]undecan-8-one which was condensed with 3-(MeO)C6H4MgBr to give, after deprotection, cis-I [R = OH, R1 = R5 = H, R2 = C6H4(OMe)-3, R3 = R4 = Me]. Data for biol. activity of I were given.

L28 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:489218 CAPLUS Full-text
DOCUMENT NUMBER: 135:71304
TITLE: Substituted 4-amino-1-phenylbutan-2-ol compounds as regulators for the nociception/orphanin FQ ligand ORL1 receptor system, their preparation, and their therapeutic use
INVENTOR(S): Sundermann, Bernd; Wnendt, Stephan; Englberger, Werner
PATENT ASSIGNEE(S): Grunenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

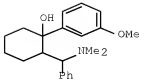
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047506	A2	20010705	WO 2000-EP12975	20001220
WO 2001047506	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19963175	A1	20010712	DE 1999-19963175	19991227
CA 2396516	A1	20010705	CA 2000-2396516	20001220
EP 1253917	A2	20021106	EP 2000-985205	20001220
EP 1253917	B1	20050216		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518491	T	20030610	JP 2001-548101	20001220
HU 2002003900	A2	20030728	HU 2002-3900	20001220
HU 2002003900	A3	20050628		
NZ 519933	A	20030829	NZ 2000-519933	20001220
AU 776229	B2	20040902	AU 2001-21688	20001220
AT 289195	T	20050315	AT 2000-985205	20001220
PT 1253917	T	20050531	PT 2000-985205	20001220
ES 2236018	T3	20050716	ES 2000-985205	20001220
US 2003008859	A1	20030109	US 2002-149434	20020624
US 7012099	B2	20060314		
MX 2002PA06398	A	20030410	MX 2002-PA6398	20020626
PRIORITY APPLN. INFO.:			DE 1999-19963175 A	19991227
			WO 2000-EP12975 W	20001220
OTHER SOURCE(S):		MARPAT 135:71304		

AB The invention relates to the use of substituted 4-amino-1-phenylbutan-2-ol compds. in the form of their racemates, enantiomers, diastereomers or corresponding bases or corresponding salts of physiol. acceptable acids, as regulators for the nociception/orphanin FQ ligand ORL1 receptor system and for the production of medicaments. The compds. of the invention may be used as anxiolytics, to treat depression, senile dementia, etc. Compds. include e.g. 1-(2-chlorobenzyl)-2-(dimethylaminophenylmethyl)cyclohexanol and its hydrochloride salt. Compound preparation is described.

L28 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:723166 CAPLUS Full-text
DOCUMENT NUMBER: 133:296270
TITLE: Preparation of 1-aryl-2-(α-aminophenylmethyl)cyclohexanols and analogs as drugs
INVENTOR(S): Sundermann, Bernd; Kogel, Babette-Yvonne; Hennies, Hagen-Heinrich; Buschmann, Helmut
PATENT ASSIGNEE(S): Grunenthal G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1043307	A2	20001011	EP 2000-104477	20000308
EP 1043307	A3	20010718		
EP 1043307	B1	20030604		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19915601	A1	20001019	DE 1999-19915601	19990407
AT 242197	T	20030615	AT 2000-104477	20000308
PT 1043307	T	20031031	PT 2000-104477	20000308
ES 2200740	T3	20040316	ES 2000-104477	20000308
NZ 503396	A	20001124	NZ 2000-503396	20000314
MX 200003285	A	20020308	MX 2000-3285	20000404
CA 2304127	A1	20001007	CA 2000-2304127	20000405
BR 2000008682	A	20020226	BR 2000-8682	20000405
HU 2000001396	A2	20020429	HU 2000-1396	20000405
NO 2000001781	A	20001009	NO 2000-1781	20000406
CN 1270162	A	20001018	CN 2000-104979	20000406
JP 2000327642	A	20001128	JP 2000-105250	20000406
ZA 2000001746	A	20001206	ZA 2000-1746	20000406
SK 285259	B6	20061005	SK 2000-496	20000406
US 6410790	B1	20020625	US 2000-545371	20000407
HK 1031725	A1	20040305	HK 2001-102345	20010331

PRIORITY APPLN. INFO.: DE 1999-19915601 A 19990407
OTHER SOURCE(S): MARPAT 133:296270
GI



II

AB HOCR2R3CHR1CHRNR4R5 [I; R = (un)substituted (hetero)aryl; R1,R2 = alkyl; R1R2 = (phenyl-substituted) C2-6 alkylene; R3 = alkyl, (hetero)aryl, phenylalkyl, etc.; R4,R5 = azetidino, pyrrolidino, piperidino, morpholino] were prepared as K- and Na-channel ligands and noradrenaline reuptake inhibitors. Thus, 2-(α-aminophenylmethyl)cyclohexanone (preparation given) was condensed with 3-(MeO)C6H4MgBr to give title compound II. Data for biol. activity of I were given.

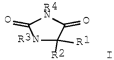
L28 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:627199 CAPLUS Full-text
DOCUMENT NUMBER: 133:276239
TITLE: Affinity, potency and efficacy of tramadol and its metabolites at the cloned human μ-opioid receptor
AUTHOR(S): Gillen, Clemens; Haurand, Michael; Kobelt, Dieter Johannes; Wnendt, Stephan
CORPORATE SOURCE: Department of Molecular Pharmacology, Grunenthal GmbH, Aachen, D-52078, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2000), 362(2), 116-121
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was conducted to characterize the centrally active analgesic drug tramadol hydrochloride [(1RS,2RS)-2-[(dimethyl-amino)- methyl]-1-(3-methoxyphenyl)-cyclohexanol hydrochloride] and its metabolites M1, M2, M3, M4 and M5 at the cloned human μ-opioid receptor. Membranes from stably transfected Chinese hamster ovary (CHO) cells were used to determine the four parameters of the ligand-receptor interaction: the affinity of (±)-tramadol and its metabolites was determined by competitive inhibition of [3H]naloxone binding under high and low salt conditions. The agonist-induced stimulation of [35S]GTPγS binding permits the measurement of potency (EC50), efficacy (Emax = maximal stimulation) and relative intrinsic efficacy (effect as a function of receptor occupation). The metabolite (+)-M1 showed the highest affinity (Ki=3.4 nM) to the human μ-opioid receptor, followed by (±)-M5 (Ki=100 nM), (-)-M1 (Ki=240 nM) and (±)-tramadol (Ki=2.4 μM). The [35S]GTPγS binding assay revealed an agonistic activity for the metabolites (+)-M1, (-)-M1 and (±)-M5 with the following rank order of intrinsic efficacy: (+)-M1>(±)-M5>(-)-M1. The metabolites (±)-M2, (±)-M3 and (±)-M4 displayed only weak affinity (Ki>10μM) and had no stimulatory effect on GTPγS binding. These data indicate that the metabolite (+)-M1 is responsible for the μ-opioid-derived analgesic effect.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:413909 CAPLUS Full-text
DOCUMENT NUMBER: 127:34212
TITLE: Preparation of substituted imidazolidin-2,4-dione derivatives as immunomodulators.
INVENTOR(S): Zimmer, Oswald; Boehlke, Horst; Wnendt, Stephan; Geist-rudolf, Cornelia; Zwingenberger, Kai
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 770613	A1	19970502	EP 1996-116069	19961008
EP 770613	B1	19990609		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 19540027	A1	19970430	DE 1995-19540027	19951027
AT 181072	T	19990615	AT 1996-116069	19961008
ES 2135148	T3	19991016	ES 1996-116069	19961008
AU 9668181	A	19970501	AU 1996-68181	19961014
AU 707751	B2	19990722		
ZA 9608956	A	19970529	ZA 1996-8956	19961024
JP 09188677	A	19970722	JP 1996-282701	19961024
HU 9602932	A2	19980728	HU 1996-2932	19961024
HU 9602932	A3	19980828		
HU 222120	B1	20030428		
CA 2188908	A1	19970428	CA 1996-2188908	19961025
US 6004963	A	19991221	US 1996-738232	19961025
IL 119488	A	20010111	IL 1996-119488	19961025
RU 2163603	C2	20010227	RU 1996-121181	19961025
PL 184446	B1	20021031	PL 1996-316706	19961025
CN 1152573	A	19970625	CN 1996-121960	19961026
CN 1097050	B	20021225		
HK 1010367	A1	20000420	HK 1998-110963	19980925

PRIORITY APPLN. INFO.: DE 1995-19540027 A 19951027
OTHER SOURCE(S): CASREACT 127:34212; MARPAT 127:34212
GI



I

AB Title compds. [I; R1 = alkyl, cycloalkyl; R2 = alkyl, Ph, phenylalkyl, (CH2)1-4CO2R5; R1R2 = (CH2)4-6, CH2CH2OCH2CH2, o-CH2C6H4CH2; R3 = H, alkyl, (CH2)1-4CO2R5; R4 = (methyl)pyridyl, pyrazinyl, methylisoxazolyl, benzothiadiazolyl, (substituted) thiadiazolyl, thiazolyl; R5 = alkyl], were prepared Thus, 2-aminothiazole in THF was treated with carbonyldiimidazole and then with Et 2-amino-2-propylpentanoate (preparation given) to give 62% Et 2-propyl-2-(3-thiazol-2-ylureido)pentanoate. This was stirred with SOCl2 to give 5,5-

dipropyl-3-thiazol-2-ylimidazolidin-2,4- dione. The latter at 50 µg/mL inhibited LPS-stimulated THFα release by 83%.

L28 ANSWER 20 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2008-A02753 [01] WPIX
DOC. NO. CPI: C2008-000480 [01]
TITLE: New 1-aminomethyl-4-oxazolylalkyl-cyclohexane derivatives, useful for treating e.g. pain, depression and urinary incontinence, bind to mu-opioid receptors
DERWENT CLASS: B02; B03
INVENTOR: ENGLBERGER W; GRAUBAUM H; MERLA B; OBERBOERSCH S; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 116

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 102005061429	A1	20070628	(200801)*	DE	56[0]	
WO 2007079928	A1	20070719	(200801)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 102005061429	A1	DE 2005-102005061429	20051222
WO 2007079928	A1	WO 2006-EP12222	20061219

PRIORITY APPLN. INFO: DE 2005-102005061429 20051222
AN 2008-A02753 [01] WPIX
AB DE 102005061429 A1 UPAB: 20080102
NOVELTY - 1-aminomethyl-4-oxazolylalkyl-cyclohexane derivatives (I), as racemates, enantiomers, diastereomers (and mixtures), bases and salts with acids are new.

DETAILED DESCRIPTION - 1-aminomethyl-4-oxadiazolylalkyl- cyclohexane derivatives of formula (I), as racemates, enantiomers, diastereomers (and mixtures), bases and salts with acids are new.

n = 0-2;

R1 = aryl or heteroaryl attached through 1-3C alkyl, both optionally substituted, one or more times;

R2 = aryl or heteroaryl, both optionally substituted, one or more times, and/or attached through a 1-3C alkyl;

R3 and R4 = 1-6C alkyl (optionally unsaturated, linear or branched, optionally substituted one or more times) or aryl (optionally substituted one or more times and/or attached through 1-3C alkyl) or together they complete a 5-7 membered ring, saturated or unsaturated (but not aromatic), optionally containing an additional heteroatom (S, O or N), optionally substituted one or more times, and the ring may be fused to an aromatic ring;

R5 and R6 = hydrogen or 1-6C alkyl (optionally unsaturated and/or branched), but are not both hydrogen, or together they complete CH2CH2OCH2CH2 or (CH2)3-6;

R7 and R8 = 1-4C alkyl (optionally unsaturated and/or substituted one or more times) or (hetero)aryl optionally substituted one or more times and attached through 1-3C alkyl, or together they form a 5-7 membered ring as defined above.

An INDEPENDENT CLAIM is included for a method for preparing (I) by reacting aldehyde (A), with amine NHR4R3 (B) and isonitrile amide NC-

CHR1CONR7R8 (C) in organic solvent, e.g. (m)ethanol, at 30-100, preferably 40-80, degreesC for 1-10 hours.

ACTIVITY - Analgesic; Antidepressant; Uropathic; Antidiarrheic; Antipruritic; Antialcoholic; Tranquilizer.

MECHANISM OF ACTION - (I) bind to the mu-opioid receptors. The compound ((4-((4-benzyl-5-pyrrolidin-1-yl-oxazol-2-yl)piperidin-1- ylmethyl)-cyclohexyl)-(4-fluorophenyl)methyl)cyclohexyl)methyl)methylpheny lamine caused 76% inhibition of the human mu receptor at a concentration of 1 muM

USE - (I) are used for treatment of pain (particularly acute, neuropathic pain); depression; urinary incontinence; diarrhea; pruritis; alcohol or drug misuse; dependence on pharmaceuticals; loss of motivation and anxiety (all claimed).

L28 ANSWER 21 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2007-849887 [79] WPIX
DOC. NO. CPI: C2007-290986 [79]
TITLE: New 1-aminomethyl-4-oxadiazolylalkyl-cyclohexane derivatives, useful for treating e.g. pain, depression and urinary incontinence, bind to mu-opioid receptors and inhibit reuptake of serotonin and noradrenaline
DERWENT CLASS: B03
INVENTOR: ENGLBERGER W; GRAUBAUM H; HENNIES H; HENNIES H H; MERLA B; OBERBOERSCH S; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 116

PATENT INFO ABBR.:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
DE 102005061427	A1 20070628	(200779)*	DE	61[0]	
WO 2007079931	A1 20070719	(200779)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 102005061427	A1	DE 2005-102005061427	20051222
WO 2007079931	A1	WO 2006-EP12225	20061219

PRIORITY APPLN. INFO: DE 2005-102005061427 20051222
AN 2007-849887 [79] WPIX
AB DE 102005061427 A1 UPAB: 20071207

NOVELTY - 1-Aminomethyl-4-oxadiazolylalkyl-cyclohexane derivatives (I), as racemates, enantiomers, diastereomers (and mixtures), bases and acid salts are new.

DETAILED DESCRIPTION - 1-Aminomethyl-4-oxadiazolylalkyl- cyclohexane derivatives of formula (I), as racemates, enantiomers, diastereomers (and mixtures), bases and acid salts are new.

X = CH, CH2, CH=CH, CH2CH2, CH2CH=CH or CH2CH2CH2;

R1 = aryl or heteroaryl, both optionally substituted, one or more times, and/or optionally attached through a 1-3C alkyl;

R2 = aryl or heteroaryl, both optionally substituted, one or more times, or optionally substituted aryl attached through a 1-3C alkyl;

R3 and R4 = hydrogen, 1-6C alkyl, optionally unsaturated, linear or branched, but not both hydrogen, or together they complete CH2CH2OCH2CH2 or (CH2)x;

x = 3-6.

An INDEPENDENT CLAIM is included for a method for preparing (I) by reacting an amidoxime (D) and ester (A) in presence of a base, particularly NaH.

ACTIVITY - Analgesic; Antidepressant; Uropathic; Antidiarrheic; Antipruritic; Antialcoholic; Tranquilizer.

MECHANISM OF ACTION - Compounds (I) (a) bind to the mu-opioid receptors and (b) inhibit reuptake of serotonin and noradrenaline. The compound (4-((3-(4-chlorobenzyl)-1,2,4-oxadiazol-5-yl)methyl)cyclohexyl)- N,N-dimethyl(phenyl)methamine caused 83% inhibition of the human mu receptor at a concentration of 1 muM, corresponding to Ki = 0.044 muM, and at 10 muM caused 95% inhibition of reuptake for both serotonin and noradrenaline.

USE - (I) are used for treatment of pain (particularly acute, neuropathic or chronic pain), depression, urinary incontinence, diarrhea, pruritis, alcohol or drug misuse, dependence on pharmaceuticals, loss of motivation and anxiety (all claimed).

L28 ANSWER 22 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-732226 [76] WPIX
DOC. NO. CPI: C2006-225585 [76]
TITLE: New 5,6,7,8-tetrahydro-imidazo(1,2-a)pyridin-2-ylamine compounds are vanilloid receptor 1 inhibitors useful to treat e.g. pain, migraine, depressions, inflammations, urinary incontinence, neurodegenerative disorders and eating disorders
DERWENT CLASS: B02
INVENTOR: FRANK R; SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 112

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 102005016547	A1	20061012	(200676)*	DE	79[0]	
WO 2006105971	A1	20061012	(200676)	DE		
EP 1869038	A1	20071226	(200803)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 102005016547	A1	DE 2005-102005016547	20050408
WO 2006105971	A1	WO 2006-EP3153	20060407
EP 1869038	A1	EP 2006-724098	20060407
EP 1869038	A1	WO 2006-EP3153	20060407

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1869038	A1	Based on	WO 2006105971	A

PRIORITY APPLN. INFO: DE 2005-102005016547 20050408
AN 2006-732226 [76] WPIX
AB DE 102005016547 A1 UPAB: 20061127
NOVELTY - 5,6,7,8-Tetrahydro-imidazo(1,2-a)pyridin-2-ylamine compounds (I) are new.

DETAILED DESCRIPTION - 5,6,7,8-Tetrahydro-imidazo(1,2-a)pyridin-2-ylamine compounds of formula (I) are new.

Either R1, R2 = e.g. H; or

NR1R2 = optionally substituted 4-9 membered heterocyclo-aliphatic group;

R3 = e.g. H or optionally substituted 1-10C aliphatic group; and

R4 = 1-10C aliphatic group, 3-9-membered cyclo-aliphatic group or 5-14-membered (hetero) aryl residue (all optionally substituted).

Full definitions are given in the 'DEFINITIONS - Full Definitions:' field. INDEPENDENT CLAIMS are included for:

(1) the preparation of (I); and

(2) a medicament comprising (I) and auxiliary materials.

ACTIVITY - Analgesic; Antidepressant; Antiinflammatory; Uropathic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Nootropic; Eating-Disorders-Gen.; Anabolic; Immunomodulator; Anorectic; Tranquilizer; Antidiarrheic; Antipruritic; Antialcoholic; Antiaddictive; Cardiovascular-Gen.

MECHANISM OF ACTION - Vanilloid receptor 1 inhibitor; Batrachotoxin binding cell of sodium channel binder; mu-Opioid receptor binder. The ability of (I) to inhibit vanilloid receptor 1 was tested using biological assays. The results showed that the percentage inhibition of 2-(butyl-(3,4-difluoro-benzoyl)-amino)-5,6,7,8-tetrahydro-imidazo(1,2- a)pyridin-3-carboxylic acid-(2-methyl-cyclohexyl)-amide was 171.

USE - (I) are useful as medicaments for the treatment and/or prevention of pain, preferably acute pain, chronic pain and neuropathic pain; migraine; depressions; inflammations; avolition; urinary incontinence; neurodegenerative disorders, preferably Parkinson disease, Huntington disease, Alzheimer disease and multiple sclerosis; eating disorders, preferably bulimia, anorexia, obesity and cachexia; fear conditions; cognitive dysfunction, preferably memory disorders; cognitive deficiency conditions (attention deficit syndrome); epilepsy; catalepsy; diarrhea and pruritus; alcohol-, drug- and/or medicine abuse, alcohol-, drug- and/or medicine dependence, preferably for reduction of withdrawal symptoms in alcohol- and/or drug dependence; for the prophylaxis and/or reduction of tolerance development medicaments, preferably medicaments based on opioid; for regulation of food intake; for the modulation of movement activity; for the regulation of cardiovascular system, local anesthesia; for increasing vigilance, libido; diuresis; or for antinatriuresis (claimed).

L28 ANSWER 23 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-445147 [45] WPIX
DOC. NO. CPI: C2006-139169 [45]
TITLE: New spirocyclic cyclohexane derivatives are noradrenaline or serotonin reuptake inhibitors useful for e.g. pain relief and treatment of depression, epilepsy, diarrhea and bulimia
DERWENT CLASS: B02
INVENTOR: HINZE C; SCHICK H; SONNENSCHEIN H; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 110

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006018184	A2	20060223	(200645)*	DE	59[0]	
DE 102004039382	A1	20060223	(200645)	DE		
EP 1778680	A2	20070502	(200731)	DE		
US 20070213351	A1	20070913	(200762)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006018184 A2		WO 2005-EP8625	20050809
DE 102004039382 A1		DE 2004-102004039382	20040813
EP 1778680 A2		EP 2005-776804	20050809
EP 1778680 A2		WO 2005-EP8625	20050809
US 20070213351 A1	Cont of	WO 2005-EP8625	20050809
US 20070213351 A1		US 2007-705096	20070212

FILING DETAILS:

PATENT NO	KIND	PATENT NO	
EP 1778680	A2 Based on	WO 2006018184	A

PRIORITY APPLN. INFO: DE 2004-102004039382 20040813
AN 2006-445147 [45] WPIX
AB WO 2006018184 A2 UPAB: 20060714
NOVELTY - Spirocyclic cyclohexane derivatives (I) and their enantiomers, diastereomers, mixtures of diastereomers and enantiomers and salts are new.

DETAILED DESCRIPTION - Spirocyclic cyclohexane derivatives of formula (I) and their enantiomers, diastereomers, mixtures of diastereomers and enantiomers and salts are new.

R1, R2 = 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl (all optionally substituted), H, formyl or AQ; or

R1+R2 = CH2CH2OCH2CH2, CH2CH2NR11CH2CH2 or (CH2)3-6;

A = 1-3C alkylene;

Q = (hetero)aryl or 3-8C cycloalkyl (both optionally substituted);

R11 = R;

R = 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl, (un)saturated 3-8C cycloalkyl, (hetero)aryl (all optionally substituted), H or AQ;

R3 = phenyl, phenethyl, thienyl, pyridyl or benzyl (all optionally substituted);

W = NR4, O or S;

R4 = 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl, (hetero)aryl (all optionally substituted), H, AQ, COR12 or SO2R12;

R12 = R, OR13 or NR14R15;

R5 = oxo, COOR13, CONR13 (sic), OR13 or R;

R6 = F, Cl, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, COOR13, NR14R15 or R; or

R5+R6 = (CH2)n (optionally substituted with F, Cl, Br, I, NO2, CF3, OR13, CN or 1-5C alkyl);

n=2-6;

R7-R10 = H, F, Cl, Br, I, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, COOR13, NR14R15, 1-5C alkyl, optionally substituted 3-8C cycloalkyl; optionally substituted (hetero)aryl or AQ;

R13 = R;

R14, R15 = R; or

R14+R15 = CH2CH2OCH2CH2, CH2CH2NR16CH2CH2 or (CH2)3-6;

R16 = 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl (all optionally substituted) or H;

X = O, S, SO, SO2 or NR17; and

R17 = 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl (all optionally substituted), H, COR12 or SO2R12.

INDEPENDENT CLAIMS are also included for four processes for preparing (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Cardiant; Vasotropic; Uropathic; Antidiarrheic; Antipruritic; Antialcoholic; Antiaddictive; Antiinflammatory; Antiarrhythmic; Antiemetic; Nootropic.

MECHANISM OF ACTION - Opioid receptor ligand; Serotonin reuptake inhibitor; Noradrenaline reuptake inhibitor. 1,1-(2-Dimethylaminomethyl-3-hydroxy-3-(3-methoxyphenyl)pentamethylene)-3,4-dihydro-1H-2,9- diazafluorene dihydrochloride (Ia) gave 44% inhibition of serotonin reuptake in the assay described in Drug Res., 46(III), 1029 (1996).

USE - (I) are useful for preparing medicaments for preventing or treating pain (particularly acute, chronic or neuropathic pain) and for preventing or treating anxiety, depression, epilepsy, cardiovascular diseases, urinary incontinence, diarrhea, pruritus, alcohol and drug abuse, drug dependence, inflammation, lack of drive, bulimia, anorexia or catalepsy or for use as local anesthetics, antiarrhythmics, antiemetics or nootropics and for increasing vigilance and libido (all claimed).

L28 ANSWER 24 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-100070 [10] WPIX
DOC. NO. CPI: C2006-035700 [10]
TITLE: New 1-acylamino-4-aminocyclohexane derivatives, useful for treatment and prevention of e.g. pain, anxiety and stress, bind to opioid receptors and modulate reuptake of noradrenalin and serotonin
DERWENT CLASS: B05
INVENTOR: SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110973	A1	20051124	(200610)*	DE	50[0]	
DE 102004023508	A1	20051208	(200610)	DE		
EP 1751090	A1	20070214	(200715)	DE		
US 20070117803	A1	20070524	(200735)	EN		
JP 2007536320	W	20071213	(200801)	JA	38	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110973	A1	WO 2005-EP4910	20050506
DE 102004023508	A1	DE 2004-102004023508	20040510
EP 1751090	A1	EP 2005-741145	20050506
EP 1751090	A1	WO 2005-EP4910	20050506
US 20070117803	A1 Cont of	WO 2005-EP4910	20050506
US 20070117803	A1	US 2006-594944	20061109
JP 2007536320	W	WO 2005-EP4910	20050506
JP 2007536320	W	JP 2007-512030	20050506

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1751090	A1	Based on	WO 2005110973	A
JP 2007536320	W	Based on	WO 2005110973	A

PRIORITY APPLN. INFO: DE 2004-102004023508 20040510
AN 2006-100070 [10] WPIX
AB WO 2005110973 A1 UPAB: 20060310

NOVELTY - 1-Acylamino-4-aminocyclohexane derivatives (I), as racemates, individual or mixed enantiomers or stereoisomers, free bases or salts with acids or cations are new.

DETAILED DESCRIPTION - 1-Acylamino-4-aminocyclohexane derivatives of formula (I), as racemates, individual or mixed enantiomers or stereoisomers, free bases or salts with acids or cations are new.

R1, R2 = H, 1-5C alkyl, linear or branched, optionally unsaturated, 3-8C cycloalkyl or, linked through 1-3C alkyl, aryl, 3-8C cycloalkyl or heteroaryl, all optionally substituted one or more times, or together they complete morpholino, 4-R10-piperazino or (CH2)x;

x = 3-6;

R10 = R1 or also (hetero)aryl, phenylcarbonyl, heteroarylcarbonyl or 1-5C alkylcarbonyl, all optionally substituted;

R3 = as defined for R1 but not hydrogen, or also optionally substituted (hetero)aryl;

A = CO or SO2;

m = 1-3;

B = (CR5R6)n, (hetero)aryl or 3-8C cycloalkyl (all optionally substituted one or more times) or, linked through 1-3C alkyl in which one C can be replaced by O, (hetero) aryl or 3-8C cycloalkyl (all optionally substituted one or more times) and the 1-3C alkyl chain can be linked to cyclic residue B and/or N, so optionally two alkyl chains are present;

n = 1-5;

R4 = COR9 or SO2R8;

R5, R6 = R3, H;

R7 = H or, with B, is a 5-7 membered ring, saturated or unsaturated, but not aromatic, and part of a polycyclic ring system;

R8 = R3;

R9 = OR3 or R3.

An INDEPENDENT CLAIM is also included for preparation of (I) by reacting a cyclohexane-1,4-diamine (II) with acid HO(A-B-NR7)m-R4 (III), in presence of coupling agents, or with the reactive derivative, preferably acyl chloride, of (III).

ACTIVITY - Analgesic; Tranquilizer; Anticonvulsant; Nootropic; Neuroprotective; Neuroleptic; Cardiant; Hypotensive; Hypertensive; Antipruritic; Auditory; Anorectic; Antidiarrheic; Uropathic; Anesthetic; Diuretic.

MECHANISM OF ACTION - Mu opioid receptor binder; ORL-1 receptor binder; Noradrenalin reuptake modulator; Serotonin reuptake modulator.

Benzyl ((1-(4-dimethylamino-4-(3-fluorophenyl)cyclohexylcarbamoyl)- 3-methylbutylcarbamoyl)methyl)carbamate gave 100% inhibition of ligand binding to mu receptors and 98% inhibition at ORL-1 receptors, when tested at 1 muM on CHO cells transformed to express the receptors.

USE - (I) are used for treatment of pain (especially acute, neuropathic and chronic), anxiety, stress and related syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, catalepsy, generalized cognitive dysfunction, learning and memory disorders, withdrawal symptoms, alcohol, drug or pharmaceutical abuse or dependence, sexual dysfunction, cardiovascular disease, hypo or hypertension, tinitus, pruritis, migrane, poor hearing, inadequate intestinal motility, eating disorders, anorexia, obesity, locomotor disorders, diarrhoea, cachexia, urinary incontinence, also as muscle relaxant, anticonvulsant or anesthetic (including combined use with opioids, analgesics and anesthetics), for diuresis and anti-natriuresis, anxiolytic, for modulating motor activity and neurotransmitter distribution and to reduce addictive potential of opioids (all claimed).

L28 ANSWER 25 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-038495 [04] WPIX
TITLE: New 4-amino cyclohexanecarboxamide derivatives are

opioid receptor ligands, serotonin and noradrenaline reuptake inhibitors, useful for treatment of e.g. pain, Alzheimer's disease and obesity
DERWENT CLASS: B05
INVENTOR: HINZE C; SCHICK H; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110977	A1	20051124	(200604)*	DE	44[0]	
DE 102004023632	A1	20051208	(200604)	DE		
EP 1751095	A1	20070214	(200715)	DE		
US 20070105941	A1	20070510	(200732)	EN		
US 7241802	B2	20070710	(200746)	EN		
JP 2007536318	W	20071213	(200801)	JA	31	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110977	A1	WO 2005-EP4908	20050506
DE 102004023632	A1	DE 2004-102004023632	20040510
EP 1751095	A1	EP 2005-745589	20050506
EP 1751095	A1	WO 2005-EP4908	20050506
US 20070105941	A1 Cont of	WO 2005-EP4908	20050506
US 7241802	B2 Cont of	WO 2005-EP4908	20050506
US 20070105941	A1	US 2006-594935	20061109
US 7241802	B2	US 2006-594935	20061109
JP 2007536318	W	WO 2005-EP4908	20050506
JP 2007536318	W	JP 2007-512028	20050506

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1751095	A1	Based on	WO 2005110977	A
JP 2007536318	W	Based on	WO 2005110977	A

PRIORITY APPLN. INFO: DE 2004-102004023632 20040510
AN 2006-038495 [04] WPIX
AB WO 2005110977 A1 UPAB: 20060227
NOVELTY - 4-Amino cyclohexanecarboxamide derivatives (I), their isomers and salts are new.

DETAILED DESCRIPTION - 4-Amino cyclohexanecarboxamide derivatives of formula (I) ,their isomers and salts are new.

R1, R2 = H, formyl, optionally substituted (un)saturated 1-5C alkyl, optionally substituted (un)saturated 3-8C cycloalkyl or AQ;

R1+R2 = (CH2)2O(CH2)2, (CH2)2NR10(CH2)2 or (CH2)3-6;

A = 1-3C alkyl;

Q = aryl, 3-8C cycloalkyl or heteroaryl, each optionally substituted;

R10 = H, optionally substituted (un)saturated 1-5C alkyl, optionally substituted (un)saturated 3-8C cycloalkyl, optionally substituted aryl or heteroaryl or AQ;

R3 = cyclopentyl, cyclohexyl, naphthyl, thienyl, benzothiophenyl, furyl, benzofuranyl, benzodioxolanyl, indolyl, indanyl, benzodioxanyl or pyridyl, each optionally substituted or A'Q';

A' = 1-2C alkyl;

Q' = 5-6C cycloalkyl, phenyl, naphthyl, anthracenyl, thienyl, benzothiophenyl, pyridyl, furyl, benzofuranyl, benzodioxolanyl, indolyl, indanyl, benzodioxanyl, pyrrolyl, pyrimidyl or pyrazinyl, each optionally substituted; or phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 4-chlorophenyl, 3-chlorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2,4-dichlorophenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2,4-difluorophenyl, 2-fluoro-3-chlorophenyl, 2-chloro-3-fluorophenyl, 2-chloro-4-fluorophenyl, 2-fluoro-4-chlorophenyl, 4-fluoro-3-chlorophenyl, 4-fluoro-3-methylphenyl, 4-t-butylphenyl, 4-fluoro-3-chlorophenyl, 4-bromo-3-fluorophenyl, 3,5- bis(trifluoromethyl)phenyl, 4-chloro-2-trifluoromethylphenyl, 2-methoxy-5-methylphenyl, 5-chloro-2-methoxyphenyl, 4-phenoxyphenyl, 2-methylthiophenyl, 3-methylthiophenyl, 4-methylthiophenyl, 5-fluoro-2-methoxyphenyl, 4-chloro-3-trifluoromethyl or 4-bromo-2-methylphenyl;

R4 = (CR6R7)nR8;

n = 0 - 6;

R6 = H or optionally substituted (un)saturated 1-5C alkyl;

R7 = H, optionally substituted (un)saturated 1-5C alkyl or COOR9;

R6+R7 = (CH2)kCHR8(CH2)m;

k = 1 -3;

m = 1 or 2;

R8 = Q;

R9 = H or optionally substituted (un)saturated 1-5C alkyl;

R5 = H or (CH2)lR8;

l = 1 - 3; and

R4+R5 = (CH2)2O(CH2)2 or (CH2)2NR10(CH2)2.

An INDEPENDENT CLAIM is also included for preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Nootropic; Neuroprotective; Antialcoholic; Antiaddictive; Vasotropic; Hypotensive; Auditory; Antipruritic; Antimigraine; Anorectic; Antidiarrheic; Immunomodulator; Uropathic; Relaxant; Endocrine-Gen; Gastrointestinal-Gen; Muscular-Gen; Cardiovascular-Gen; Hypertensive; Eating-Disorders-Gen; Anesthetic; Diuretic.

MECHANISM OF ACTION - Opioid receptor ligand; Serotonin reuptake inhibitor; Noradrenaline reuptake inhibitor.

N-(3-phenylpropyl)-4-dimethylamino-4-phenyl-cyclohexanecarboxamide hydrochloride (Ia) (nonpolar diastereomer) was found to exhibit 88% inhibition of serotonin reuptake at a concentration of 1 muM in the assay described in Drug Res., 46(III), 1029 (1996).

USE - (I) Are useful for preparing medicaments for preventing or treating pain; for preparing medicaments for preventing or treating anxiety, stress, depression, catalepsy, epilepsy, Alzheimer's disease, senile dementia, cognitive dysfunction, withdrawal symptoms, alcohol and drug abuse, sexual dysfunction, cardiovascular diseases, hypotension, hypertension, tinnitis, pruritis, migraine, hearing difficulties, deficient intestinal motility, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence; as muscle relaxants, anticonvulsants or anesthetics; for coadministration with opioid analgesics or anesthetics; for diuresis or antinatriuresis; for modulating neurotransmitter secretion and thus treating neurodegenerative diseases, treating withdrawal symptoms and/or reducing the addictive potential of opioids (all claimed).

L28 ANSWER 26 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN

ACCESSION NUMBER: 2006-038494 [04] WPIX
TITLE: New cyclohexylacetamide derivatives are opioid receptor ligands, serotonin and noradrenaline reuptake inhibitors, useful for the treatment of e.g. pain, senile dementia and depression
DERWENT CLASS: B05
INVENTOR: HENKEL B; HINZE C; SCHICK H; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110976	A1	20051124	(200604)*	DE	90[0]	
DE 102004023507	A1	20051201	(200604)	DE		
EP 1751093	A1	20070214	(200715)	DE		
US 20070129347	A1	20070607	(200738)	EN		
JP 2007536319	W	20071213	(200801)	JA	61	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110976 A1		WO 2005-EP4909	20050506
DE 102004023507 A1		DE 2004-102004023507	20040510
EP 1751093 A1		EP 2005-745355	20050506
EP 1751093 A1		WO 2005-EP4909	20050506
US 20070129347 A1	Cont of	WO 2005-EP4909	20050506
US 20070129347 A1		US 2006-594945	20061109
JP 2007536319 W		WO 2005-EP4909	20050506
JP 2007536319 W		JP 2007-512029	20050506

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1751093	A1	Based on	WO 2005110976	A
JP 2007536319	W	Based on	WO 2005110976	A

PRIORITY APPLN. INFO: DE 2004-102004023507 20040510
AN 2006-038494 [04] WPIX
AB WO 2005110976 A1 UPAB: 20060227
NOVELTY - Cyclohexylacetamide derivatives (I), their isomers and salts are new.

DETAILED DESCRIPTION - Cyclohexylacetamide derivatives of formula (I), their isomers and salts are new.

R1, R2 = H, formyl, optionally substituted (un)saturated 1-5C alkyl, optionally substituted (un)saturated 3-8C cycloalkyl, or AQ;

R1+R2 = (CH2)2O(CH2)2, (CH2)2NR10(CH2)2 or (CH2)3-6;

A = 1-3C alkyl;

Q = aryl, 3-8C cycloalkyl or heteroaryl (both optionally substituted);

R10 = H, optionally substituted (un)saturated 1-5C alkyl, optionally substituted (un)saturated 3-8C cycloalkyl, optionally substituted aryl or heteroaryl, or AQ;

R3 = optionally substituted (un)saturated 1-5C alkyl, optionally substituted (un)saturated 3-8C cycloalkyl, AQ or Q';

Q' = naphthyl, anthracenyl, thienyl, benzothiophenyl, pyridyl, furyl, benzofuranyl, benzodioxolanyl, indolyl, indanyl, benzodioxanyl, pyrrolyl, pyrimidyl or pyrazinyl (all optionally substituted), phenyl, 2-fluorophenyl,

3-fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 4-chlorophenyl, 3-chlorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2,4-dichlorophenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2,4-difluorophenyl, 2-fluoro-3-chlorophenyl, 2-chloro-3-fluorophenyl, 2-chloro-4-fluorophenyl, 2-fluoro-4-chlorophenyl, 4-fluoro-3-chlorophenyl, 4-fluoro-3-methylphenyl, 4-t-butylphenyl, 4-fluoro-3-chlorophenyl, 4-bromo-3-fluorophenyl, 3,5-bis(trifluoromethyl)phenyl, 4-chloro-2-trifluoromethylphenyl, 2-methoxy-5-methylphenyl, 5-chloro-2-methoxyphenyl, 4-phenoxyphenyl, 2-methylthiophenyl, 3-methylthiophenyl, 4-methylthiophenyl, 5-fluoro-2-methoxyphenyl, 4-chloro-3-trifluoromethyl or 4-bromo-2-methylphenyl;

R4 = (CR6R7)nR8;

n = 0 - 6;

R6 = H or optionally substituted (un)saturated 1-5C alkyl;

R7 = H, optionally substituted (un)saturated 1-5C alkyl or COOR9;

R6+R7 = (CH2)kCHR8(CH2)m;

k = 1-3;

m = 1 or 2;

R8 = Q;

R9 = H or optionally substituted (un)saturated 1-5C alkyl;

R5 = H or (CH2)lR8;

l = 1-3;

R4+R5 = (CH2)2O(CH2)2 ,(CH2)3-6 or (CH2)2NR10(CH2)2; and

a = single or double bond.

An INDEPENDENT CLAIM is also included for preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Nootropic; Neuroprotective; Antialcoholic; Antiaddictive; Vasotropic; Hypotensive; Auditory; Antipruritic; Antimigraine; Anorectic; Antidiarrheic; Immunomodulator; Uropathic; Relaxant; Endocrine-Gen; Cardiovascular-Gen; Hypertensive; Gastrointestinal-Gen; Eating-Disorders-Gen; Muscular-Gen; Anesthetic; Antidiuretic.

MECHANISM OF ACTION - Opioid receptor ligand; Serotonin reuptake inhibitor; Noradrenaline reuptake inhibitor.

2-(4-Dimethylamino-4-phenylcyclohexylidene)-N-(2-(1H-indol-3-yl)ethyl)acetamide hydrochloride (Ia) was found to exhibit 96% inhibition of serotonin reuptake at a concentration of 1 muM in the assay described in Drug Res., 46(III), 1029 (1996).

USE - (I) Are useful for preparing medicaments for preventing or treating pain; for preparing medicaments for preventing or treating anxiety, stress, depression, catalepsy, epilepsy, Alzheimer's disease, senile dementia, cognitive dysfunction, withdrawal symptoms, alcohol and drug abuse, sexual dysfunction, cardiovascular diseases, hypotension, hypertension, tinnitis, pruritis, migraine, hearing difficulties, deficient intestinal motility, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence; as muscle relaxants, anticonvulsants or anesthetics; for coadministration with opioid analgesics or anesthetics; for diuresis or antinatriuresis; for modulating neurotransmitter secretion and thus treating neurodegenerative diseases, treating withdrawal symptoms and/or reducing the addictive potential of opioids (all claimed).

L28 ANSWER 27 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-038493 [04] WPIX
TITLE: New 1-acylamino-4-~~amino~~cyclohexane derivatives are opioid receptor antagonists, noradrenalin and serotonin

reuptake modulators, useful for treatment and prevention of e.g. pain, anxiety and stress
DERWENT CLASS: B05
INVENTOR: SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110975	A1	20051124	(200604)*	DE	74[0]	
DE 102004023506	A1	20051201	(200604)	DE		
EP 1747191	A1	20070131	(200712)	DE		
US 20070281954	A1	20071206	(200781)	EN		
JP 2007536322	W	20071213	(200801)	JA	68	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110975	A1	WO 2005-EP4912	20050506
DE 102004023506	A1	DE 2004-102004023506	20040510
EP 1747191	A1	EP 2005-747800	20050506
EP 1747191	A1	WO 2005-EP4912	20050506
US 20070281954	A1 Cont of	WO 2005-EP4912	20050506
US 20070281954	A1	US 2006-594953	20061109
JP 2007536322	W	WO 2005-EP4912	20050506
JP 2007536322	W	JP 2007-512032	20050506

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1747191	A1	Based on	WO 2005110975	A
JP 2007536322	W	Based on	WO 2005110975	A

PRIORITY APPLN. INFO: DE 2004-102004023506 20040510
AN 2006-038493 [04] WPIX
AB WO 2005110975 A1 UPAB: 20060227
NOVELTY - 1-Acylamino-4-aminocyclohexane derivatives (I), their racemates, individual or mixed enantiomers or stereoisomers, free bases or salts with acids or cations are new.

DETAILED DESCRIPTION - 1-Acylamino-4-aminocyclohexane derivatives of formula (I), their racemates, individual or mixed enantiomers or stereoisomers, free bases or salts with acids or cations are new.

R1 and R2 = hydrogen, 1-5C alkyl, linear or branched, optionally unsaturated, 3-8C cycloalkyl, 1-3C alkyl, aryl, 3-8C cycloalkyl or heteroaryl, all optionally substituted, or together they form morpholino, 4-R10-piperazino or (CH2)x;

x = 3 - 6;

R10 = as defined for R1 or also (hetero)aryl, phenylcarbonyl, heteroarylcarbonyl or 1-5C alkylcarbonyl, all optionally substituted;

R3 and R4 = as defined for R1, but not hydrogen, or also optionally substituted (hetero)aryl;

X = (CR5R6)n or optionally substituted (hetero)aryl, linked through optionally substituted 1-3C alkyl;

n = 0 - 4;

A = NH, ON (and then there is a double bond between N and R4), O or S;

l = 1 or 2;

R4 = as defined for R1 other than hydrogen, or also (hetero)aryl, optionally substituted;

R5 and R6 = hydrogen, 1-5C alkyl (linear or branched, optionally unsaturated) or aryl, each optionally substituted;

Provided that X is not heteroaryl when l = 1 and A = O or S.

An INDEPENDENT CLAIM is also included for preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Anticonvulsant; Nootropic; Neuroprotective; Neuroleptic; Cardiant; Hypotensive; Hypertensive; Antipruritic; Auditory; Anorectic; Antidiarrheic; Uropathic; Anesthetic; Diuretic; Antidepressant; Antialcoholic; Antiaddictive; Endocrine-Gen; Cardiovascular-Gen; Antimigraine; Gastrointestinal-Gen; Eating-Disorders-Gen; Muscular-Gen.

MECHANISM OF ACTION - Opioid receptor antagonists (mu and ORL-1 receptors); Noradrenalin and serotonin reuptake modulators.

2-(4-Dimethylamino-4-(3-methylbenzyl)cyclohexylcarbamoyl)benzyl benzoate (Ia) was found to exhibit 106% inhibition of ligand binding to mu receptors and 44% inhibition at ORL-1 receptors, when tested at 1 muM on chinese hamster ovary (CHO) cells transformed to express the receptors.

USE - (I) Are useful for treatment of pain (especially acute, neuropathic and chronic); anxiety; stress and related syndromes; depression; epilepsy; Alzheimer's disease; senile dementia; catalepsy; generalized cognitive dysfunction; learning and memory disorders; withdrawal symptoms; alcohol, drug or pharmaceutical abuse or dependence; sexual dysfunction; cardiovascular disease; hypo- or hyper-tension; tinnitus; pruritis; migraine; poor hearing; inadequate intestinal motility; eating disorders; anorexia; obesity; locomotor disorders; diarrhoea; cachexia; urinary incontinence; also as muscle relaxant, anticonvulsant or anesthetic (including combined use with opioids, analgesics and anesthetics); for diuresis and anti-natriuresis; anxiolytic; for modulating motor activity and neurotransmitter distribution and to reduce addictive potential of opioids (all claimed).

L28 ANSWER 28 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-038492 [04] WPIX
TITLE: New 1-aminoacylalkanoylamino-4-aminocyclohexane derivatives, useful for treatment and prevention of e.g. pain, anxiety and stress, bind to opioid receptors and modulate reuptake of noradrenalin and serotonin
DERWENT CLASS: B03; B05
INVENTOR: SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110974	A1	20051124	(200604)*	DE	93[0]	
DE 102004023522	A1	20051201	(200604)	DE		
EP 1745010	A1	20070124	(200708)	DE		
US 20070112007	A1	20070517	(200734)	EN		
JP 2007536323	W	20071213	(200801)	JA	86	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110974	A1	WO 2005-EP4913	20050506
DE 102004023522	A1	DE 2004-102004023522	20040510
EP 1745010	A1	EP 2005-739598	20050506

EP 1745010 A1	WO 2005-EP4913 20050506
US 20070112007 A1 Cont of	WO 2005-EP4913 20050506
US 20070112007 A1	US 2006-594963 20061109
JP 2007536323 W	WO 2005-EP4913 20050506
JP 2007536323 W	JP 2007-512033 20050506

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1745010	A1	Based on	WO 2005110974	A
JP 2007536323	W	Based on	WO 2005110974	A

PRIORITY APPLN. INFO: DE 2004-102004023522 20040510
AN 2006-038492 [04] WPIX
AB WO 2005110974 A1 UPAB: 20060227

NOVELTY - 1-aminoacylalkylanoyllamino-4-aminocyclohexane derivatives (I), as racemates; individual or mixed enantiomers or stereoisomers; free bases or salts with acids or cations are new.

DETAILED DESCRIPTION - 1-aminoacylalkanolylamino-4- aminocyclohexane derivatives of formula (I), as racemates; individual or mixed enantiomers or stereoisomers; free bases or salts with acids or cations are new.

n = 1-5;

R1 and R2 = hydrogen, 1-5C alkyl, linear or branched, optionally unsaturated, 3-8C cycloalkyl or, linked through 1-3C alkyl, aryl, 3-8C cycloalkyl or heteroaryl, all optionally substituted one or more times, or together they complete morpholino, 4-R10-piperazino or (CH2)x;

x = 3-6;

R10 = R1 or also (hetero)aryl, phenylcarbonyl, heteroarylcarbonyl or 1-5C alkylcarbonyl, all optionally substituted;

R3 = R1, but not hydrogen;

R4 = -(CR6R7)pR8;

R5 = hydrogen or -(CH2)lR8 or together with R4 forms CH2CHR14OCHR14CH2, CH2CH2(S or NR11)CH2CH2, (CR12R13)x or -CH2CH2C(R12)=CH-CH2-;

p = 0-4;

R6 = hydrogen or 1-5C alkyl, linear or branched, saturated or unsaturated and optionally substituted one or more times;

R7 = as defined for R6 or also COOR9, or with R6 forms (CH2)kCHR8(CH2)m;

k = 1-3;

m = 1-2;

R8 = 1-6C alkyl (saturated or unsaturated, linear or branched, optionally substituted one or more times) or, all optionally substituted one or more times, 3-8C cycloalkyl or (hetero)aryl;

R9 = hydrogen or 1-5C alkyl;

l = 1-3;

R11 = R1 or (hetero)aryl, optionally substituted one or more times;

R12 = R11 or hydroxy or benzoyl (optionally substituted one or more times);

R13 = hydrogen or hydroxy, or together with R12, on the same or adjacent C atom, forms a 5-6 membered ring, optionally containing heteroatoms, saturated or unsaturated, optionally substituted and/or part of a polycyclic system; and

R14 = hydrogen or 1-3C alkyl, optionally unsaturated, linear or branched and optionally substituted one or more times.

An INDEPENDENT CLAIM is also included for two methods for preparing (I).

ACTIVITY - Analgesic; Tranquilizer; Anticonvulsant; Nootropic; Neuroprotective; Neuroleptic; Cardiant; Hypotensive; Hypertensive;

Antipruritic; Auditory; Anorectic; Antidiarrheic; Uropathic; Anesthetic; Diuretic.

MECHANISM OF ACTION - Mu opioid receptor; ORL-1 receptor.

N-(1-(2,6-dichlorobenzyl)pyrrolidin-3-yl)-N'-(4-dimethylamino-4-(4-methylbenzyl)cyclohexylsuccinamide gave 93% inhibition of serotonin uptake and 71% inhibition of noradrenaline uptake when tested at 1 muM on rat synpasosomes.

USE - (I) are used for treatment of pain (especially acute, neuropathic and chronic); anxiety; stress and related syndromes; depression; epilepsy; Alzheimer's disease; senile dementia; catalepsy; generalized cognitive dysfunction; learning and memory disorders; withdrawal symptoms; alcohol, drug or pharmaceutical abuse or dependence; sexual dysfunction; cardiovascular disease; hypo- or hyper-tension; tinitus; pruritis; migrane; poor hearing; inadequate intestinal motility; eating disorders; anorexia; obesity; locomotor disorders; diarrhoea; cachexia; urinary incontinence; also as muscle relaxant, anticonvulsant or anesthetic (including combined use with opioids, analgesics and anesthetics); for diuresis and anti-natriuresis; anxiolytic; for modulating motor activity and neurotransmitter distribution and to reduce addictive potential of opioids (all claimed).

L28 ANSWER 29 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-038490 [04] WPIX
TITLE: New 1-heteroarylacylamino-4-aminocyclohexane derivatives, useful for treatment and prevention of e.g. pain, anxiety and stress, bind to opioid receptors and modulate reuptake of noradrenalin and serotonin
DERWENT CLASS: B05
INVENTOR: SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110971	A1	20051124	(200604)*	DE	62[0]	
DE 102004023635	A1	20060413	(200626)	DE		
EP 1745009	A1	20070124	(200708)	DE		
US 20070129369	A1	20070607	(200738)	EN		
JP 2007536321	W	20071213	(200801)	JA	49	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110971	A1	WO 2005-EP4911	20050506
DE 102004023635	A1	DE 2004-102004023635	20040510
EP 1745009	A1	EP 2005-759144	20050506
EP 1745009	A1	WO 2005-EP4911	20050506
US 20070129369	A1 Cont of	WO 2005-EP4911	20050506
US 20070129369	A1	US 2006-595003	20061109
JP 2007536321	W	WO 2005-EP4911	20050506
JP 2007536321	W	JP 2007-512031	20050506

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1745009	A1 Based on	WO 2005110971 A

JP 2007536321 W Based on WO 2005110971 A

PRIORITY APPLN. INFO: DE 2004-102004023635 20040510
AN 2006-038490 [04] WPIX
AB WO 2005110971 A1 UPAB: 20060227
NOVELTY - 1-Heteroarylacylamino-4-aminocyclohexane derivatives (I), as racemates; individual or mixed enantiomers or stereoisomers; free bases or salts with acids or cations are new.

DETAILED DESCRIPTION - 1-Heteroacylamino-4-aminocyclohexane derivatives of formula (I), as racemates; individual or mixed enantiomers or stereoisomers; free bases or salts with acids or cations are new.

R1 and R2 = H, 1-5C alkyl, linear or branched, optionally unsaturated, 3-8C cycloalkyl or, linked through 1-3C alkyl, aryl, 3-8C cycloalkyl or heteroaryl, all optionally substituted one or more times, or together they complete morpholino, 4-R10-piperazino or (CH2)x;

x = 3-6;

R10 = R1,(hetero)aryl, phenylcarbonyl, heteroarylcarbonyl or 1-5C alkylcarbonyl, all optionally substituted;

R3 = as defined for R1 but not H, or also optionally substituted (hetero)aryl;

A = heteroaryl, optionally substituted one or more times;

B = (CH2)m, SO2, O, S, CO or CS;

m = 0 or 1;

R4 = (hetero)aryl, optionally linked through a 1-3C alkyl chain, optionally substituted one or more times.

An INDEPENDENT CLAIM is also included for preparation of (I) by reacting a cyclohexane-1,4-diamine (II) with acid HOOC-A-B-R4 (III), in presence of coupling agents, or with the reactive derivative, preferably acyl chloride, of (III).

ACTIVITY - Analgesic; Tranquilizer; Anticonvulsant; Nootropic; Neuroprotective; Neuroleptic; Cardiant; Hypotensive; Hypertensive; Antipruritic; Auditory; Anorectic; Antidiarrheic; Uropathic; Anesthetic; Diuretic.

MECHANISM OF ACTION - mu Opioid receptor modulator; ORL-1 opioid receptor modulator; Noradrenalin reuptake modulator; Serotonin reuptake modulator. N-(4-dimethylamino-4-phenylcyclohexyl) 5-methyl-2-phenyl-2H- 1,2,3-triazole-4-carboxamide gave 100% inhibition of ligand binding to mu receptors and 88% inhibition at ORL-1 receptors, when tested at 1 muM on CHO cells transformed to express the receptors.

USE - (I) are used for treatment of pain (especially acute, neuropathic and chronic); anxiety; stress and related syndromes; depression; epilepsy; Alzheimer's disease; senile dementia; catalepsy; generalized cognitive dysfunction; learning and memory disorders; withdrawal symptoms; alcohol, drug or pharmaceutical abuse or dependence; sexual dysfunction; cardiovascular disease; hypo- or hyper-tension; tinitus; pruritis; migrane; poor hearing; inadequate intestinal motility; eating disorders; anorexia; obesity; locomotor disorders; diarrhoea; cachexia; urinary incontinence; also as muscle relaxant, anticonvulsant or anesthetic (including combined use with opioids, analgesics and anesthetics); for diuresis and anti-natriuresis; anxiolytic; for modulating motor activity and neurotransmitter distribution and to reduce addictive potential of opioids (all claimed).

L28 ANSWER 30 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-038489 [04] WPIX
TITLE: New 1-acylamino-4-aminocyclohexane derivatives, useful for treatment and prevention of e.g. pain, anxiety and stress, bind to opioid receptors and modulate reuptake of noradrenalin and serotonin
DERWENT CLASS: B05

INVENTOR: SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 109

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005110970	A1	20051124	(200604)*	DE	44[0]	
DE 102004023501	A1	20051201	(200604)	DE		
EP 1751088	A1	20070214	(200715)	DE		
US 20070088034	A1	20070419	(200729)	EN		
JP 2007536317	W	20071213	(200801)	JA	34	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005110970 A1		WO 2005-EP4907	20050506
DE 102004023501 A1		DE 2004-102004023501	20040510
EP 1751088 A1		EP 2005-738450	20050506
EP 1751088 A1		WO 2005-EP4907	20050506
US 20070088034 A1	Cont of	WO 2005-EP4907	20050506
US 20070088034 A1		US 2006-594952	20061109
JP 2007536317 W		WO 2005-EP4907	20050506
JP 2007536317 W		JP 2007-512027	20050506

FILING DETAILS:

PATENT NO	KIND	PATENT NO	
EP 1751088	A1 Based on	WO 2005110970	A
JP 2007536317	W Based on	WO 2005110970	A

PRIORITY APPLN. INFO: DE 2004-102004023501 20040510
AN 2006-038489 [04] WPIX
AB WO 2005110970 A1 UPAB: 20060227

NOVELTY - 1-acylamino-4-aminocyclohexane derivatives (I), as racemates, individual or mixed enantiomers or stereoisomers, free bases or salts with acids or cations are new.

DETAILED DESCRIPTION - 1-acylamino-4-aminocyclohexane derivatives of formula (I), as racemates, individual or mixed enantiomers or stereoisomers, free bases or salts with acids or cations are new.

R1, R2 = H, 1-5C alkyl, linear or branched, optionally unsaturated, 3-8C cycloalkyl or, linked through 1-3C alkyl, aryl, 3-8C cycloalkyl or heteroaryl, all optionally substituted one or more times, or together they complete morpholino, 4-R10-piperazino or (CH2)x;

x = 3-6;

R10 = as defined for R1 or also (hetero)aryl, phenylcarbonyl, heteroarylcarbonyl or 1-5C alkylcarbonyl, all optionally substituted;

R3 and R4 = as defined for R1, but not hydrogen, or also optionally substituted (hetero)aryl;

X = (CH2)n, linear or branched, aryl, 3-8C cycloalkyl, or aryl or 3-8C cycloalkyl linked through 1-3C alkyl, all optionally substituted;

n = 0-5.

An INDEPENDENT CLAIM is also included for preparation of (I) by reacting a cyclohexane-1,4-diamine (II) with acid derivative HOOC.X.COR4 (III), in presence of coupling agents, or with the reactive derivative, preferably acyl chloride, of (III).

ACTIVITY - Analgesic; Tranquilizer; Anticonvulsant; Nootropic; Neuroprotective; Neuroleptic; Cardiant; Hypotensive; Hypertensive; Antipruritic; Auditory; Anorectic; Antidiarrheic; Uropathic; Anesthetic; Diuretic.

MECHANISM OF ACTION - Opioid receptor modulators; mu-opioid receptor modulator; ORL-1 opioid receptor modulator; Noradrenalin reuptake modulator; Serotonin reuptake modulator.

5-oxo-5-phenyl-valeric acid (4-dimethylamino-4- phenylcyclohexylamide) gave 100% inhibition of ligand binding to both mu and ORL-1 receptors, when tested at 1 muM on CHO cells transformed to express the receptors.

USE - (I) are used for treatment of pain (especially acute, neuropathic and chronic); anxiety; stress and related syndromes; depression; epilepsy; Alzheimer's disease; senile dementia; catalepsy; generalized cognitive dysfunction; learning and memory disorders; withdrawal symptoms; alcohol, drug or pharmaceutical abuse or dependence; sexual dysfunction; cardiovascular disease; hypo- or hyper-tension; tinitus; pruritis; migrane; poor hearing; inadequate intestinal motility; eating disorders; anorexia; obesity; locomotor disorders; diarrhoea; cachexia; urinary incontinence; also as muscle relaxant, anticonvulsant or anesthetic (including combined use with opioids, analgesics and anesthetics); for diuresis and anti-natriuresis; anxiolytic; for modulating motor activity and neurotransmitter distribution and to reduce addictive potential of opioids (all claimed).

L28 ANSWER 31 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-618524 [63] WPIX
DOC. NO. CPI: C2005-185970 [63]
TITLE: New 2-acylamino-tetrahydrobenzothiazole derivatives, useful e.g. for treatment or prevention of pain, alcohol misuse, inflammation and depression, inhibit reuptake of serotonin and noradrenaline
DERWENT CLASS: B02
INVENTOR: BIJSTERVELD E; OBERBOERSCH S; SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005077924	A1	20050825	(200563)*	DE	160[0]	
DE 102004006808	A1	20050901	(200563)	DE		
EP 1716128	A1	20061102	(200672)	DE		
US 20070027315	A1	20070201	(200712)	EN		
JP 2007522171	W	20070809	(200754)	JA	104	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005077924	A1	WO 2005-EP1369	20050211
DE 102004006808	A1	DE 2004-102004006808	20040211
EP 1716128	A1	EP 2005-715296	20050211
EP 1716128	A1	WO 2005-EP1369	20050211
US 20070027315	A1 Cont of	WO 2005-EP1369	20050211
US 20070027315	A1	US 2006-502456	20060811
JP 2007522171	W	WO 2005-EP1369	20050211
JP 2007522171	W	JP 2006-552551	20050211

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1716128	A1	Based on	WO 2005077924	A
JP 2007522171	W	Based on	WO 2005077924	A

PRIORITY APPLN. INFO: DE 2004-102004006808 20040211
AN 2005-618524 [63] WPIX
AB WO 2005077924 A1 UPAB: 20051223
NOVELTY - 2-acylamino-4,5,6,7-tetrahydrobenzothiazole derivatives (I), as pure stereoisomers (especially enantiomers or diastereoisomers), racemates or mixtures of stereoisomers in all proportions, optionally as salts or solvates are new.

DETAILED DESCRIPTION - 2-acylamino-4,5,6,7-tetrahydrobenzothiazole derivatives of formula (I), as pure stereoisomers (especially enantiomers or diastereoisomers), racemates or mixtures of stereoisomers in all proportions, optionally as salts or solvates are new.

R1 = NR3R4 or NR5R6;

R2 = linear, branched, saturated or unsaturated aliphatic residue, optionally substituted at least once; a saturated or unsaturated cycloaliphatic residue (optionally substituted at least once and optionally with at least one heteroatom in the ring), or a (hetero)aryl, optionally substituted at least once, where cycloaliphatic and (hetero)aryl groups may be attached through an alkylene, alkenylene or alkynylene group, itself optionally substituted at least once and/or including at least one heteroatom;

R3 and R4 each = as R1 or hydrogen;

R5 and R6 together with N = saturated, unsaturated or aromatic heterocycle, optionally substituted at least once and optionally with at least one extra heteroatom in the ring.

An INDEPENDENT CLAIM is also included for prepartion of (I) from 4-ethoxycarbonyl-2-amino-4,5,6,7-tetrahydrobenzothiazole (II) by acylation; hydrolysis of ester to free acid, then conversion of this to amide.

ACTIVITY - Analgesic; Antialcohol; Antiinflammatory; Antidepressant; Anorectic; Immunomodulator; Tranquilizer.

MECHANISM OF ACTION - (I) bind to 5-hydroxytryptophan (5HT) and noradrenaline receptors, so inhibit reuptake of these compounds. The compound N-(1-(2,6-dichlorobenzyl)pyrrolidin-3-yl)-N-methyl 2-(2-cyclohexylacetylamino)-4,5,6,7-tetrahydrobenzothiazole-4-carboxamide was tested on isolated rat brain synaptosomes and at 10 muM produced 97% inhibition of 5HT reuptake and 42% inhibition of noradrenaline reuptake.

USE - (I) are used for regulating reuptake of noradrenaline and 5-hydroxytryptophan so are useful for treating and/or preventing pain; alcohol or drug misuse/addiction; inflammation; depression; lassitude; appetite disorders (particularly bulimia, anorexia, obesity and cachexia); also to increase awareness and libido, and as anxiolytic (all claimed).

L28 ANSWER 32 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-597693 [61] WPIX
DOC. NO. CPI: C2005-179907 [61]
TITLE: New spiro-(cyclohexane-tricyclic heterocyclyl)-amine derivatives, are opioid receptor ligands useful e.g. for treating pain, anxiety, stress, epilepsy, cognitive dysfunction or drug dependence
DERWENT CLASS: B02
INVENTOR: HENKEL B; HINZE C; SCHICK H; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005063769	A1	20050714	(200561)*	DE	45[0]	
DE 10360793	A1	20050728	(200561)	DE		
US 20050187281	A1	20050825	(200561)	EN		
EP 1697379	A1	20060906	(200659)	DE		
JP 2007515447	W	20070614	(200741)	JA	28	
US 7288560	B2	20071030	(200772)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005063769	A1	WO 2004-EP14540	20041221
DE 10360793	A1	DE 2003-10360793	20031223
EP 1697379	A1	EP 2004-804137	20041221
EP 1697379	A1	WO 2004-EP14540	20041221
JP 2007515447	W	WO 2004-EP14540	20041221
US 20050187281	A1	US 2004-19416	20041223
JP 2007515447	W	JP 2006-546041	20041221
US 7288560	B2	US 2004-19416	20041223

FILING DETAILS:

PATENT NO	KIND	PATENT NO	
EP 1697379	A1 Based on	WO 2005063769	A
JP 2007515447	W Based on	WO 2005063769	A

PRIORITY APPLN. INFO: DE 2003-10360793 20031223
AN 2005-597693 [61] WPIX
AB WO 2005063769 A1 UPAB: 20051223
NOVELTY - Spiro-(cyclohexane-tricyclic heterocyclyl)-amine derivatives (I), e.g. N-(1',3',4',5'-tetrahydro-spiro-(cyclohexane-1,1'- pyrano-(4,3-b)-indol)-4-yl)-amine derivatives, are new.

DETAILED DESCRIPTION - Spiro-cyclic cyclohexylamine derivatives of formula (I) (as racemate, enantiomers, diastereomers or mixtures of enantiomers or diastereomers) and their salts with acids or cations are new.

R1, R2 = H, CHO, Alk, Cyc, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

or R1 + R2 = (CH2)2O(CH2)2, (CH2)2N(R11)(CH2)2 or (CH2)3-6;

Alk = optionally substituted (os), optionally unsaturated 1-5C alkyl;

Cyc = os, optionally unsaturated 3-8C cycloalkyl;

Ar = os aryl;

Het = os heteroaryl;

Cyc' = os 3-8C cycloalkyl;

R11 = H, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

R3 = Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

W = NR4, O or S;

R4 = H, Alk, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl, Het-(1-3C) alkyl, COR12 or SO2R12;

R12 = H, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl, Het-(1-3C) alkyl, OR13 or NR14R15;

R5 = =O, H, COOR13, CONR13, OR13, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

R6 = H, F, Cl, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, COOR13, NR14R15, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

or R5 + R6 = (CH2)n (os by by one or more of halo, NO2, CF3, OR13, CN or 1-5C alkyl);

R7 - R10 = H, halo, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, COOR13, NR14R15, 1-5C alkyl, Cyc', Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

R13 - R15 = H, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

or R14 + R15 = (CH2)2O(CH2)2, (CH2)2N(R16)(CH2)2 or (CH2)3-6;

R16 = H or Alk;

X = O, S, SO, SO2 or NR17;

R17 = H, optionally unsaturated 1-5C alkyl, COR12 or SO2R12.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Analgesic; tranquilizer; antidepressant; anticonvulsant; neuroprotective; nootropic; antiaddicitive; antialcoholic; vasotropic; cardiant; hypotensive; hypertensive; auditory; antipruritic; antimigraine; laxative; anorectic; antidiarrheic; immunomodulator; uropathic; relaxants; anesthetics; diuretic; antidiuretic.

MECHANISM OF ACTION - Opioid-like receptor 1 (ORL-1) ligand; psi-opiate receptor ligand; batrachotoxin (BTX) binding site ligand. More generally (I) act on the opioid receptor system. In receptor binding assays the citrate of N,N-dimethyl-N-(4-pyridine-1',3',4',5'-tetrahydro- spiro-(cyclohexane-1,1'-pyrano-(4,3-b)-indol)-4-yl)-amine (Ia) showed 49% inhibition of the ORL-1 receptor at 1 muM, 78% inhibition of the mu-receptor at 1 muM and 84% inhibition of the BTX receptor at 10 muM.

USE - (I) are used as medicaments, specifically:

(1) for treating pain (especially acute, neuropathic or chronic pain), anxiety states, stress and associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory disorders (i.e. as nootropic agents), withdrawal symptoms, alcohol, drug or medicament abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, gastric motility deficiency, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence;

(2) muscle relaxants, anesthetics, local anesthetics, diuretics, antidiuretics or anxiolytic agents;

(3) agents for co-administration in treatment with opioid analgesics or anesthetics; or

(4) for modulating movement activity, modulating neurotransmitter release (and treating associated neurodegenerative diseases), treating withdrawal symptoms and reducing the addiction potential of opioids.

L28 ANSWER 33 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-571113 [58] WPIX
DOC. NO. CPI: C2005-172750 [58]
TITLE: New spiro-(cyclohexane-tricyclic heterocyclyl)-amine derivatives, are opioid-like receptor 1 (ORL-1) ligands useful e.g. for treating pain, anxiety, stress, epilepsy, cognitive dysfunction or drug dependence
DERWENT CLASS: B03
INVENTOR: ENGLBERGER W; FRIDERICHS E; FRIEDERICHS E; FROMANN S; FRORMANN S; HENKEL B; HINZE C; KOEGEL B; KOEGEL B Y; KOGEL B; LINZ K; MERLA B; OBERBEORSCH E; OBERBOERSCH S; OBERBORSCH S; OBERBORSCHI S; SAUNDERS D; SCHICK H; SCHRODER W; SCHROEDER W; SONNENSCHEIN H; SUNDERMANN B; SUNERMANN B; KOGEL B Y
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH

COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005066183	A1	20050721	(200558)*	DE	55[0]	
DE 10360792	A1	20050728	(200558)	DE		
US 20050192333	A1	20050901	(200558)	EN		
NO 2006003422	A	20060925	(200670)	NO		
EP 1725567	A1	20061129	(200680)	DE		
MX 2006007171	A1	20060901	(200706)	ES		
AU 2004312147	A1	20050721	(200707)	EN		
JP 2007515446	W	20070614	(200741)	JA	35	
CN 1922189	A	20070228	(200743)	ZH		
IN 2006KN01854	P2	20070511	(200746)	EN		
KR 2007014117	A	20070131	(200755)	KO		
ZA 2006006067	A	20071031	(200781)	EN	54	
US 7332519	B2	20080219	(200816)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005066183	A1	WO 2004-EP14539	20041221
DE 10360792	A1	DE 2003-10360792	20031223
AU 2004312147	A1	AU 2004-312147	20041221
CN 1922189	A	CN 2004-80042036	20041221
EP 1725567	A1	EP 2004-804136	20041221
NO 2006003422	A	WO 2004-EP14539	20041221
EP 1725567	A1	WO 2004-EP14539	20041221
MX 2006007171	A1	WO 2004-EP14539	20041221
JP 2007515446	W	WO 2004-EP14539	20041221
IN 2006KN01854	P2	WO 2004-EP14539	20041221
KR 2007014117	A	WO 2004-EP14539	20041221
US 20050192333	A1	US 2004-19372	20041223
JP 2007515446	W	JP 2006-546040	20041221
MX 2006007171	A1	MX 2006-7171	20060622
IN 2006KN01854	P2	IN 2006-KN1854	20060704
KR 2007014117	A	KR 2006-714815	20060721
ZA 2006006067	A	ZA 2006-6067	20060721
NO 2006003422	A	NO 2006-3422	20060724
US 7332519	B2	US 2004-19372	20041223

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1725567	A1	Based on	WO 2005066183	A
MX 2006007171	A1	Based on	WO 2005066183	A
AU 2004312147	A1	Based on	WO 2005066183	A
JP 2007515446	W	Based on	WO 2005066183	A
KR 2007014117	A	Based on	WO 2005066183	A

PRIORITY APPLN. INFO: DE 2003-10360792 20031223
AN 2005-571113 [58] WPIX
AB WO 2005066183 A1 UPAB: 20051223
NOVELTY - Spiro-(cyclohexane-tricyclic heterocyclyl)-amine derivatives (I) are new.

DETAILED DESCRIPTION - Spiro-cyclic cyclohexylamine derivatives of formula (I) (as racemate, enantiomers, diastereomers or mixtures of enantiomers or diastereomers) and their salts with acids or cations are new.

R1, R2 = H, CHO, Alk, Cyc, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

or R1 + R2 = (CH2)2O(CH2)2, (CH2)2N(R11)(CH2)2 or (CH2)3-6;

Alk = optionally substituted (os), optionally unsaturated 1-5C alkyl;

Cyc = os, optionally unsaturated 3-8C cycloalkyl;

Cyc' = os 3-8C cycloalkyl;

Ar = os aryl;

Het = os heteroaryl;

Cyc' = os 3-8C cycloalkyl;

R11 = H, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

R3 = Het or Het-(1-3C) alkyl;

W' = NR4, O or S;

R4 = H, Alk, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl, Het-(1-3C) alkyl, COR12 or SO2R12;

R12 = H, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl, Het-(1-3C) alkyl, OR13 or NR14R15;

R5 = =O, H, COOR13, CONR13, OR13, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

R6 = H, F, Cl, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, COOR13, NR14R15, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

or R5 + R6 = (CH2)n (os by by one or more of halo, NO2, CF3, OR13, CN or 1-5C alkyl);

n = 2-6;

R7 - R10 = H, halo, NO2, CF3, OR13, SR13, SO2R13, SO2OR13, CN, COOR13, NR14R15, 1-5C alkyl, Cyc', Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

R13 - R15 = H, Alk, Cyc, Ar, Het, Ar-(1-3C) alkyl, Cyc'-(1-3C) alkyl or Het-(1-3C) alkyl;

or R14 + R15 = (CH2)2O(CH2)2, (CH2)2N(R16)(CH2)2 or (CH2)3-6;

R16 = H or Alk;

X = O, S, SO, SO2 or NR17; and

R17 = H, optionally unsaturated 1-5C alkyl, COR12 or SO2R12.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Neuroprotective; Nootropic; Antiaddicitive; Antialcoholic; Vasotropic; Cardiant; Hypotensive; Hypertensive; Auditory; Antipruritic; Antimigraine; Laxative; Anorectic; Antidiarrheic; Immunomodulator; Uropathic; Relaxant; Anesthetic; Diuretic; Endocrine-Gen., Cardiovascular-Gen., Anabolic; Eating - Disorder-Gen.

The citrate of 1,1-(3-dimethylamino-3-(2-thienyl)-pentamethylene)-1,3,4,9-tetrahydropyrano-(3,4-b)-indole (non-polar diastereomer) (Ia) had ED50 3.5 micrograms/kg i.v. in the mouse tail-flick test for analgesic activity.

MECHANISM OF ACTION - Opioid-like receptor 1 (ORL-1) ligand; mu-opiate receptor ligand.

More generally (I) act on the opioid receptor system, especially on the ORL-1 receptor. In receptor binding assays (Ia) had Ki 0.26 nM for inhibition of the ORL-1 receptor and Ki 0.27 nM for inhibition of the mu-receptor.

USE - (I) are used as medicaments, specifically:

(1) for treating pain (especially acute, neuropathic or chronic pain);

(2) for treating alcohol, drug or medicament abuse and/or dependence;

(3) muscle relaxants or anesthetics;

(4) agents for co-administration in treatment with opioid analgesics or anesthetics, treating withdrawal symptoms and/or reducing the addiction potential of opioids;

(5) agents for treating anxiety states, stress and associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory disorders (i.e. as nootropic agents), sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, gastric motility deficiency, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence;

(6) as diuretics, antinatriuretics or anxiolytic agents; or

(7) for modulating movement activity and modulating neurotransmitter release (and treating associated neurodegenerative diseases) (all claimed).

L28 ANSWER 34 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-417845 [42] WPIX
DOC. NO. CPI: C2005-128119 [42]
TITLE: Medicaments for treating anxiety disorders and adjuvants for standard antidepressants, comprising C-(2-phenyl-cyclohexyl)-methylamine compounds
DERWENT CLASS: B05
INVENTOR: BLOMS-FUNKE P; ENGLBERGER W; HENNIES H; HENNIES H H
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005051375	A1	20050609	(200542)*	DE	35[0]	
DE 10356362	A1	20050623	(200542)	DE		
EP 1686984	A1	20060809	(200652)	DE		
US 20060258741	A1	20061116	(200677)	EN		
JP 2007512288	W	20070517	(200735)	JA	23	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005051375	A1	WO 2004-EP13439	20041126
DE 10356362	A1	DE 2003-10356362	20031128
EP 1686984	A1	EP 2004-819227	20041126
EP 1686984	A1	WO 2004-EP13439	20041126
US 20060258741	A1 Cont of	WO 2004-EP13439	20041126
US 20060258741	A1	US 2006-440005	20060525
JP 2007512288	W	WO 2004-EP13439	20041126
JP 2007512288	W	JP 2006-540395	20041126

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1686984	A1	Based on	WO 2005051375	A
JP 2007512288	W	Based on	WO 2005051375	A

PRIORITY APPLN. INFO: DE 2003-10356362 20031128
AN 2005-417845 [42] WPIX
AB WO 2005051375 A1 UPAB: 20051222
NOVELTY - The use of eleven specific C-(2-phenyl-cyclohexyl)-methylamine compounds (I) (all preferably in 1R,2R-enantiomer form), e.g. 3-(2-dimethylaminomethyl-cyclohexyl)-phenol (Ia) or (2-(3-methoxyphenyl)-

cyclohexylmethyl)-dimethylamine, as medicaments for treating anxiety disorders or as adjuvant for standard antidepressants is new.

DETAILED DESCRIPTION - The use of C-(2-phenyl-cyclohexyl)- methylamine compounds (I) is claimed in the production of medicaments for treating anxiety disorders and in the production of adjuvants for standard antidepressants. (I) is selected from 3-(2-dimethylaminomethyl- cyclohexyl)-phenol (Ia), (2-(3-methoxyphenyl)-cyclohexylmethyl)- dimethylamine, sulfuric acid mono-(3-(2-dimethylaminomethyl-cyclohexyl)- phenyl) ester, 3-(2-methylaminomethyl-cyclohexyl)-phenol, 3-(2-dimethylaminomethyl-cyclohexyl)-phenol N-oxide, 6-(3-(2-dimethylaminomethyl-cyclohexyl)-phenoxy)-3,4,5-trihydroxy- tetrahydropyran-2-carboxylic acid, 4-(2-dimethylaminomethyl-cyclohexyl)- catechol, 3-(2-aminomethyl-cyclohexyl)-phenol, C-(2-(3-methoxyphenyl)- cyclohexyl)-methylamine, (2-(3-methoxyphenyl)-cyclohexylmethyl)- methylamine and (2-(3-methoxyphenyl)-cyclohexylmethyl)-dimethylamine N-oxide. All compounds are optionally in the form of racemates or pure stereoisomers (specifically enantiomers or diastereomers) or their mixtures in all proportions; and/or in the form of salts or solvates (specifically hydrates). (I) are preferably in 1R,2R-enantiomer form.

ACTIVITY - Tranquilizer; antidepressant; analgesic.

In 'elevated plus maze' tests for anxiolytic activity in rats (see Psychopharmagcology, 2002, 163, 121-141), 3-(2-dimethylaminomethyl-cyclohexyl)-phenol (Ia) gave residence time of 118.2 seconds at a dose of 16 mg/kg, compared with 16.8 seconds in vehicle-only controls.

MECHANISM OF ACTION - psi-Opiate agonist; serotonin reuptake inhibitor; noradrenaline reuptake inhibitor.

(Ia) had Ki values of 0.14 muM, 0.05 muM and 0.16 muM in mu-opioid affinity, serotonin reuptake inhibiting and noradrenaline reuptake inhibiting assays respectively.

USE - (I) are specifically used for treatment of anxiety disorders in humans or other mammals (preferably by administration of (I) at the first onset of the disorders); or (where (I) is an adjuvant for standard antidepressants) for treating anxiety disorders or depression (all claimed).

ADVANTAGE - (I) are potent mu-opiate receptor agonists which inhibit reuptake of serotonin and noradrenaline, and in particular show a good balance between mu-opioid and monoamine reuptake inhibiting actions. They have a more rapid onset of action than conventional monoamine reuptake inhibiting anxiolytic and antidepressant drugs, and are free of anxiogenic effects. (I) also potentiate the anxiolytic and antidepressant effects of serotonin and noradrenaline reuptake inhibitors, and provide an effective therapy of drug-resistant anxiety and depression. (I) additionally show analgesic activity, and may be effective in combating pain simultaneously with the anxiety or depression.

L28 ANSWER 35 OF 47	WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER:	2004-412728 [39] WPIX
DOC. NO. CPI:	C2004-155149 [39]
TITLE:	New spiro-((cyclohexane)-tetrahydropyrano-(3,4-b)-indole) derivatives, are ORL1 receptor ligands useful e.g. for treating anxiety, depression, epilepsy, senile dementia, withdrawal symptoms or especially pain
DERWENT CLASS:	B02
INVENTOR:	AULENBACHER O; ENGELBERGER W; ENGLBERGER W; ENGLBERGER W G; FRIDERICHS E; FRIDERICHS E J; HENKEL B; HINZE C; KOEGEL B; KOEGEL B Y; KOGEL B; KOGEL B Y; LINZ K; LIPKIN M J; OBERBOERSCH S; OBERBORSCH S; OBERDOERSCH S; ROSE V S; SCHICK H; SONNENSCHEIN H; SUNDERMANN B; OBERBOERSH S
PATENT ASSIGNEE:	(CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT:	106

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10252667	A1	20040527	(200439)*	DE	15[0]	
WO 2004043967	A1	20040527	(200439)	DE		
AU 2003296563	A1	20040603	(200470)	EN		
EP 1560835	A1	20050810	(200552)	DE		
NO 2005002761	A	20050607	(200557)	NO		
BR 2003015296	A	20050830	(200558)	PT		
US 20060004034	A1	20060105	(200603)	EN		
JP 2006508114	W	20060309	(200620)	JA	70	
CN 1735619	A	20060215	(200643)	ZH		
KR 2005074579	A	20050718	(200643)	KO		
ZA 2005004725	A	20060830	(200662)	EN	137	
NZ 540575	A	20071130	(200801)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10252667 A1		DE 2002-10252667	20021111
AU 2003296563 A1		AU 2003-296563	20031105
BR 2003015296 A		BR 2003-15296	20031105
CN 1735619 A		CN 2003-80108583	20031105
EP 1560835 A1		EP 2003-810963	20031105
WO 2004043967 A1		WO 2003-EP12305	20031105
EP 1560835 A1		WO 2003-EP12305	20031105
NO 2005002761 A		WO 2003-EP12305	20031105
BR 2003015296 A		WO 2003-EP12305	20031105
US 20060004034 A1	Cont of	WO 2003-EP12305	20031105
JP 2006508114 W		WO 2003-EP12305	20031105
KR 2005074579 A		WO 2003-EP12305	20031105
JP 2006508114 W		JP 2004-550924	20031105
KR 2005074579 A		KR 2005-708319	20050510
US 20060004034 A1		US 2005-126139	20050511
NO 2005002761 A		NO 2005-2761	20050607
ZA 2005004725 A		ZA 2005-4725	20050609
NZ 540575 A		NZ 2003-540575	20031105
NZ 540575 A		WO 2003-EP12305	20031105

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003296563	A1	Based on	WO 2004043967	A
EP 1560835	A1	Based on	WO 2004043967	A
BR 2003015296	A	Based on	WO 2004043967	A
JP 2006508114	W	Based on	WO 2004043967	A
KR 2005074579	A	Based on	WO 2004043967	A
NZ 540575	A	Based on	WO 2004043967	A

PRIORITY APPLN. INFO: DE 2002-10252667 20021111
AN 2004-412728 [39] WPIX
AB DE 10252667 A1 UPAB: 20060323
NOVELTY - Spiro-((4-amino-cyclohexane)-1,1'-1',3',4',9'- tetrahydropyrano-(3,4-b)-indole) derivatives (I) are new.
DETAILED DESCRIPTION - Spiro-cyclic cyclohexylamine derivatives of formula (I), optionally in the form of racemates, pure stereoisomers

(especially enantiomers or diastereomers) or their mixtures in all proportions, including free bases, free acids, salts (specifically acid or base addition salt) or solvates (specifically hydrates), are new.

R1, R2 = H, optionally unsaturated, optionally mono- or polysubstituted 1-4C alkyl or CHO;

R3 = -(CH2)n-Aryl;

n = 0-2;

R4 = H, optionally unsaturated, optionally mono- or polysubstituted 1-3C alkyl or -CO-(CH2)m-H;

m = 0-2;

R5 - R8 = H; 1-5C alkyl or 1-3C alkoxy (both optionally unsaturated and optionally mono- or polysubstituted); or halo, OH, SH, SMe, OMe, NH2, COOH, COOMe, NHMe, NMe2 or NO2.

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Neuroprotective; Nootropic; Antiaddictive; Antialcoholic; Vasotropic; Cardiant; Hypotensive; Hypertensive; Auditory; Antipruritic; Antimigraine; Laxative; Anorectic; Antidiarrheic; Immunomodulator; Uropathic; Relaxant; Anesthetic; Diuretic.

The hydrochloride of the non-polar diastereomer of 1,1-(3-dimethylamino-3-phenyl-pentamethylene)-1,3,4,9-tetrahydropyrano- (3,4-b)-indole) (Ia) had analgesic ED50 3.5 micro-M i.v. in the mouse tail-flick test.

MECHANISM OF ACTION - Nociceptin/ORL1 receptor (opioid receptor like-receptor 1) system modulator; ORL1 receptor ligand.

USE - (I) are used as:

(1) medicaments for treating pain (especially acute, visceral, neuropathic or chronic pain), anxiety states, stress (and associated syndromes), depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory disorders (nootropic action), withdrawal syndromes, alcohol, drug or medicament abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, deficient gastric motility, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence;

(2) as muscle relaxants, anticonvulsants or anesthetics;

(3) for coadministration with opioid analgesics or anesthetics;

(4) for diuresis, antinatriuresis, anxiolysis or modulation of movement activity;

(5) for modulating neurotransmitter release and treating associated neurodegenerative diseases; or

(6) treating withdrawal syndromes and/or reducing the addiction potential of opioids (all claimed).

(I) are especially used as analgesics.

ADVANTAGE - (I) bind with the ORL1 receptor and other medicinally relevant opiate receptors; and have low toxicity.

L28 ANSWER 36 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-411679 [38] WPIX
DOC. NO. CPI: C2004-154602 [38]
TITLE: New 4-alkoxymethyl-cyclohexylamine derivatives, useful as e.g. ORL1 receptor ligands for treating e.g. anxiety, depression, epilepsy, senile dementia, withdrawal symptoms or especially pain
DERWENT CLASS: B05
INVENTOR: HINZE C; SCHICK H; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 102

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004043902	A1	20040527	(200438)*	DE	38[0]	
DE 10253323	A1	20040527	(200438)	DE		
DE 10252872	A1	20040729	(200449)	DE		
AU 2003296564	A1	20040603	(200470)	EN		
EP 1560807	A1	20050810	(200552)	DE		
US 20050267218	A1	20051201	(200579)	EN		
US 7232847	B2	20070619	(200741)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004043902	A1	WO 2003-EP12312	20031105
DE 10252872	A1	DE 2002-10252872	20021112
DE 10253323	A1	DE 2002-10253323	20021114
AU 2003296564	A1	AU 2003-296564	20031105
EP 1560807	A1	EP 2003-810964	20031105
EP 1560807	A1	WO 2003-EP12312	20031105
US 20050267218	A1 Cont of	WO 2003-EP12312	20031105
US 20050267218	A1	US 2005-126306	20050511
US 7232847	B2 Cont of	WO 2003-EP12312	20031105
US 7232847	B2	US 2005-126306	20050511

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003296564 A1	Based on	WO 2004043902 A
EP 1560807 A1	Based on	WO 2004043902 A

PRIORITY APPLN. INFO: DE 2002-10253323 20021114
DE 2002-10252872 20021112

AN 2004-411679 [38] WPIX

AB WO 2004043902 A1 UPAB: 20060203
NOVELTY - 1-Substituted 4-alkoxymethyl-cyclohexylamine derivatives (I) are new.

DETAILED DESCRIPTION - Cyclohexylamine derivatives of formula (I), optionally in the form of racemates, pure stereoisomers (especially enantiomers or diastereomers) or their mixtures in all proportions, including free bases, free acids, salts (specifically acid or base addition salt) or solvates (specifically hydrates), are new;

R1, R2 = H, Alk, Cyc, Ar, Het, -Q1-Ar, -Q1-Cyc' or -Q1-Het;

or NR1R2 = morpholino, 4-(R6)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;

Alk = optionally unsaturated, optionally mono- or polysubstituted 1-8C alkyl;

Cyc = optionally unsaturated, optionally mono- or polysubstituted 3-8C cycloalkyl;

Cyc' = optionally mono- or polysubstituted 3-8C cycloalkyl;

Ar = optionally mono- or polysubstituted aryl;

Het = optionally mono- or polysubstituted heteroaryl;

Q1 = 1-3C alkylene;

R6 = as for R1;

R3 = Alk, Cyc, Ar, Het, -Q2-Ar, -Q2-Cyc' or -Q2-Het ;

Q2 = optionally unsaturated, optionally substituted 1-4C alkylene;

R5 = Cyc', Ar, Het, -CH2R12, -(CH2)2R12 or -(CH2)3R12;

R12 = Cyc', Ar or Het.

INDEPENDENT CLAIMS are also included for the preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Neuroprotective; Nootropic; Antiaddictive; Antialcoholic; Vasotropic; Cardiant; Hypotensive; Hypertensive; Auditory; Antipruritic; Antimigraine; Laxative; Anorectic; Antidiarrheic; Immunomodulator; Uropathic; Relaxant; Anesthetic; Diuretic.

The non-polar diastereomer of (4-benzyloxymethyl-1- phenylcyclohexyl)-dimethylamine hydrochloride (Ia) had analgesic ED50 87 mg/kg i.v. in the mouse tail-flick test.

MECHANISM OF ACTION - Nociceptin/ORL1 Receptor (opioid receptor like-receptor 1) System Modulator; ORL1 Receptor Ligand. The non-polar diastereomer of (Ia) had Ki 26 nM in ORL1 receptor binding assays.

USE - (I) Are used:

(1) as medicaments for treating pain (especially acute, visceral, neuropathic or chronic pain), anxiety states, stress (and associated syndromes), depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory disorders (nootropic action), withdrawal syndromes, alcohol, drug or medicament abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, deficient gastric motility, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence;

(2) as muscle relaxants, anticonvulsants or anesthetics;

(3) for co-administration with opioid analgesics or anesthetics;

(4) for diuresis, antinatriuresis, anxiolysis or modulation of movement activity;

(5) for modulating neurotransmitter release and treating associated neurodegenerative diseases; or

(6) for treating withdrawal syndromes and/or reducing the addiction potential of opioids (all claimed).

(I) Are especially used as analgesics.

ADVANTAGE - (I) Bind strongly with the ORL1 receptor.

L28 ANSWER 37 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-411678 [38] WPIX

DOC. NO. CPI: C2004-154601 [38]

TITLE: New 4-(alkyl, alkenyl or alkynyl)-cyclohexylamine derivatives, are ORL1 receptor ligands useful e.g. for treating anxiety, depression, epilepsy, senile dementia, withdrawal symptoms or especially pain

DERWENT CLASS: B05

INVENTOR: HINZE C; SCHICK H; SUNDERMANN B

PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH

COUNTRY COUNT: 102

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004043900	A2	20040527	(200438)*	DE	40[0]	
DE 10253322	A1	20040527	(200438)	DE		
DE 10252874	A1	20040916	(200460)	DE		
AU 2003287995	A1	20040603	(200470)	EN		
EP 1560806	A2	20050810	(200552)	DE		
US 20050267107	A1	20051201	(200579)	EN		
EP 1560806	B1	20070110	(200705)	DE		
DE 50306277	G	20070222	(200725)	DE		
ES 2279195	T3	20070816	(200758)	ES		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004043900 A2		WO 2003-EP12314	20031105
DE 10252874 A1		DE 2002-10252874	20021112
DE 10253322 A1		DE 2002-10253322	20021114
AU 2003287995 A1		AU 2003-287995	20031105
DE 50306277 G		DE 2003-506277	20031105
EP 1560806 A2		EP 2003-779847	20031105
EP 1560806 B1		EP 2003-779847	20031105
DE 50306277 G		EP 2003-779847	20031105
EP 1560806 A2		WO 2003-EP12314	20031105
US 20050267107 A1	Cont of	WO 2003-EP12314	20031105
EP 1560806 B1		WO 2003-EP12314	20031105
DE 50306277 G		WO 2003-EP12314	20031105
US 20050267107 A1		US 2005-127170	20050512
ES 2279195 T3		EP 2003-779847	20031105

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
DE 50306277	G	Based on	EP 1560806	A
AU 2003287995	A1	Based on	WO 2004043900	A
EP 1560806	A2	Based on	WO 2004043900	A
EP 1560806	B1	Based on	WO 2004043900	A
DE 50306277	G	Based on	WO 2004043900	A
ES 2279195	T3	Based on	EP 1560806	A

PRIORITY APPLN. INFO: DE 2002-10253322 20021114
DE 2002-10252874 20021112

AN 2004-411678 [38] WPIX

AB WO 2004043900 A2 UPAB: 20060203
NOVELTY - 1-Substituted 4-(omega-substituted alkyl, alkenyl or alkynyl)-cyclohexylamine derivatives (I) are new.

DETAILED DESCRIPTION - Cyclohexylamine derivatives of formula (I), optionally in the form of racemates, pure stereoisomers (especially enantiomers or diastereomers) or their mixtures in all proportions, including free bases, free acids, salts (specifically acid or base addition salt) or solvates (specifically hydrates), are new.

----- = optional bond;

R1, R2 = H, Alk, Cyc, Ar, Het, -Q1-Ar, -Q1-Cyc' or -Q1-Het;

or NR1R2 = morpholino, 4-(R6)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;

Alk = optionally unsaturated, optionally mono- or polysubstituted 1-8C alkyl;

Cyc = optionally unsaturated, optionally mono- or polysubstituted 3-8C cycloalkyl;

Cyc' = optionally mono- or polysubstituted 3-8C cycloalkyl;

Ar = optionally mono- or polysubstituted aryl;

Het = optionally mono- or polysubstituted heteroaryl;

Q1 = 1-3C alkylene;

R6 = as for R1;

R3 = Alk, Cyc, Ar, Het, -Q2-Ar, -Q2-Cyc' or -Q2-Het ;

Q2 = optionally unsaturated, optionally substituted 1-4C alkylene;

R4 = H or optionally protected hydroxy;

n = 0 or 1;

R5 = Cyc', Ar, Het, -CH2R12, -(CH2)2R12 or -(CH2)3R12;

R12 = Cyc', Ar or Het.

INDEPENDENT CLAIMS are also included for the preparation of (I).

ACTIVITY - Analgesic; tranquilizer; antidepressant; anticonvulsant; neuroprotective; nootropic; antiaddictive; antialcoholic; vasotropic; cardiant; hypotensive; hypertensive; auditory; antipruritic; antimigraine; laxative; anorectic; antidiarrheic; immunomodulator; uropathic; relaxant; anesthetic; diuretic. The least polar diastereomer of dimethyl-(1-phenyl-4-(2-p-tolyl-vinyl)-cyclohexylamine hydrochloride (Ia) gave 100% inhibition at a dose of 10 mg/kg i.v. in the mouse writhing test for analgesic activity.

MECHANISM OF ACTION - Nociceptin/ORL1 receptor (opioid receptor like-receptor 1) system modulator; ORL1 receptor ligand; mu-opiate receptor ligand. The least polar diastereomer of (Ia) had Ki values of 200 nM and 42 microM respectively in ORL1 and mu-receptor binding assays.

USE - (I) are used as:

(1) medicaments for treating pain (especially acute, visceral, neuropathic or chronic pain), anxiety states, stress (and associated syndromes), depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory disorders (nootropic action), withdrawal syndromes, alcohol, drug or medicament abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, deficient gastric motility, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence;

(2) as muscle relaxants, anticonvulsants or anesthetics;

(3) for coadministration with opioid analgesics or anesthetics;

(4) for diuresis, antinatriuresis, anxiolysis or modulation of movement activity;

(5) for modulating neurotransmitter release and treating associated neurodegenerative diseases; or

(6) treating withdrawal syndromes and/or reducing the addiction potential of opioids (all claimed).

(I) are especially used as analgesics.

ADVANTAGE - (I) bind with the ORL1 receptor and other medicinally relevant receptors such as the mu-receptor.

L28 ANSWER 38 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-204310 [20] WPIX
DOC. NO. CPI: C2004-080742 [20]
TITLE: New metabolites of 3-(2-dimethylaminomethyl-cyclohexyl)-phenol, e.g. the 2-methylaminomethyl analog, useful for treating depression, elevated compulsion to urinate or urinary incontinence
DERWENT CLASS: B05
INVENTOR: BUSCHMANN H; BUSCHMANN H H; ENGLBERGER W; ENGLBERGER W G; FRIDERICHS E; FRIDERICHS E J; HARTONO R; HENNIES H; HENNIES H H; HOLENZ J; JAHNEL U; KRAUSE G; SAUNDERS D; SAUNDERS D J; STRASSBURGER W; STRASSBURGER W W A; ZIMMER O; ZIMMER O K; ENGLEBERGER W
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH; (KRAU-I) KRAUSE G
COUNTRY COUNT: 102

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10233048	A1	20040129	(200420)*	DE	14[2]	
WO 2004009067	A1	20040129	(200420)	DE		
AU 2003263179	A1	20040209	(200450)	EN		
BR 2003012854	A	20050419	(200528)	PT		
NO 2005000861	A	20050217	(200530)	NO		
EP 1530462	A1	20050518	(200533)	DE		

KR 2005019909	A	20050303	(200545)	KO	
US 20050182131	A1	20050818	(200555)	EN	
CN 1697651	A	20051116	(200620)	ZH	
JP 2006511453	W	20060406	(200625)	JA	25
MX 2005000791	A1	20051101	(200625)	ES	
ZA 2005001428	A	20060927	(200669)	EN	47
NZ 538224	A	20070531	(200738)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10233048 A1		DE 2002-10233048	20020719
AU 2003263179 A1		AU 2003-263179	20030716
BR 2003012854 A		BR 2003-12854	20030716
CN 1697651 A		CN 2003-821863	20030716
EP 1530462 A1		EP 2003-765006	20030716
WO 2004009067 A1		WO 2003-EP7720	20030716
BR 2003012854 A		WO 2003-EP7720	20030716
NO 2005000861 A		WO 2003-EP7720	20030716
EP 1530462 A1		WO 2003-EP7720	20030716
US 20050182131 A1	Cont of	WO 2003-EP7720	20030716
JP 2006511453 W		WO 2003-EP7720	20030716
MX 2005000791 A1		WO 2003-EP7720	20030716
JP 2006511453 W		JP 2004-522472	20030716
KR 2005019909 A		KR 2005-701008	20050119
MX 2005000791 A1		MX 2005-791	20050119
US 20050182131 A1		US 2005-37038	20050119
NO 2005000861 A		NO 2005-861	20050217
ZA 2005001428 A		ZA 2005-1428	20050217
NZ 538224 A		NZ 2003-538224	20030716
NZ 538224 A		WO 2003-EP7720	20030716

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003263179	A1	Based on	WO 2004009067	A
BR 2003012854	A	Based on	WO 2004009067	A
EP 1530462	A1	Based on	WO 2004009067	A
JP 2006511453	W	Based on	WO 2004009067	A
MX 2005000791	A1	Based on	WO 2004009067	A
NZ 538224	A	Based on	WO 2004009067	A

PRIORITY APPLN. INFO: DE 2002-10233048 20020719
AN 2004-204310 [20] WPIX
AB DE 10233048 A1 UPAB: 20060121
NOVELTY - Ten specific metabolites (I) of 3-(2-dimethylaminomethyl-cyclohexyl)-phenol (A) are new compounds, e.g. sulfuric acid mono-(3-(2-dimethylaminomethyl-cyclohexyl)-phenyl) ester; 3-(2-methylaminomethyl-cyclohexyl)-phenol; 3-(2-dimethylaminomethyl- cyclohexyl)-phenol N-oxide; and 6-(3-(2-dimethylaminomethyl-cyclohexyl)- phenoxy)-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid.

DETAILED DESCRIPTION - The following metabolites (I) of 3-(2-dimethylaminomethyl-cyclohexyl)-phenol (A) are new:

(a) sulfuric acid mono-(3-(2-dimethylaminomethyl-cyclohexyl)- phenyl) ester;

(b) 3-(2-methylaminomethyl-cyclohexyl)-phenol;

(c) 3-(2-dimethylaminomethyl-cyclohexyl)-phenol N-oxide;

(d) 6-(3-(2-dimethylaminomethyl-cyclohexyl)-phenoxy)-3,4,5- trihydroxy-tetrahydropyran-2-carboxylic acid;

(e) 4-(2-dimethylaminomethyl-cyclohexyl)-catechol;

(f) 3-(2-aminomethyl-cyclohexyl)-phenol;

(g) 4-(2-dimethylaminomethyl-cyclohexyl)-benzene-1,2-diol;

(h) C-(2-(3-methoxyphenyl)-cyclohexyl)-methylamine;

(i) (2-(3-methoxyphenyl)-cyclohexylmethyl)-methylamine; and

(j) (2-(3-methoxyphenyl)-cyclohexylmethyl)-dimethylamine N-oxide.

(I) are all optionally in the form of racemates, pure stereoisomers (especially enantiomers or diastereomers) or their mixtures in all proportions; and in free base, free acid, salt or solvate (specifically hydrate) form. Preferably (I) are in the form of the R,R-stereoisomer, especially the (1R,2R)-stereoisomers.

An INDEPENDENT CLAIM is included for the use of (A) or (I) (including e.g. stereoisomers, salts, especially the (1R,2R)- stereoisomers) in the production of medicaments for treating depression.

ACTIVITY - Antidepressant; Uropathic; Analgesic; Antiinflammatory.

In tail suspension tests for antidepressant activity in mice pretreated with 1.0 mg/kg i.v. of naxolone, (1R,2R)-(A) hydrochloride at 21.5 mg/kg i.p. reduced the immobility duration by 90%.

MECHANISM OF ACTION - mu-Opioid receptor ligand; Noradrenaline and/or Serotonin Reuptake Inhibitor.

USE - (A) and (I) are used for treating depression; and (I) are also used for treatment of elevated compulsion to urinate or urinary incontinence (all claimed). (A) is a known analgesic and (I) may additionally show analgesic action, so that (A) and (I) are especially useful for the simultaneous therapy of depression.

ADVANTAGE - (A) and (I) are effective at low doses causing no significant side-effects.

L28 ANSWER 39 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-422751 [40] WPIX
DOC. NO. CPI: C2003-111618 [40]
TITLE: New quinolin-2-one derivatives, useful for treating e.g. chronic and neuropathic pain, neurodegenerative diseases, epilepsy, schizophrenia, Tourette syndrome, encephalomyelitis, tinnitus, migraine and stroke
DERWENT CLASS: B02
INVENTOR: BUSCHMANN H; BUSCHMANN H H; ENGLBERGER W; ENGLBERGER W G; KOEGEL B; PRZEWOSNY M; SATTLEGGER M; SCHICK H
PATENT ASSIGNEE: (BUSC-I) BUSCHMANN H; (ENGL-I) ENGLBERGER W; (CHEF-C) GRUENENTHAL GMBH; (KOEG-I) KOEGEL B; (PRZE-I) PRZEWOSNY M; (SATT-I) SATTLEGGER M; (SCHI-I) SCHICK H
COUNTRY COUNT: 100

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10153347	A1	20030508	(200340)*	DE	23[0]	
WO 2003037870	A1	20030508	(200340)	DE		
EP 1442021	A1	20040804	(200451)	DE		
AU 2002346861	A1	20030512	(200464)	EN		
US 20040224980	A1	20041111	(200475)	EN		
HU 2004001831	A2	20041228	(200506)	HU		
JP 2005511567	W	20050428	(200530)	JA	59	
MX 2004004090	A1	20040701	(200545)	ES		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10153347 A1		DE 2001-10153347	20011029
AU 2002346861 A1		AU 2002-346861	20021023
EP 1442021 A1		EP 2002-782979	20021023
WO 2003037870 A1		WO 2002-EP11833	20021023
EP 1442021 A1		WO 2002-EP11833	20021023
US 20040224980 A1	Cont of	WO 2002-EP11833	20021023
HU 2004001831 A2		WO 2002-EP11833	20021023
JP 2005511567 W		WO 2002-EP11833	20021023
MX 2004004090 A1		WO 2002-EP11833	20021023
JP 2005511567 W		JP 2003-540152	20021023
HU 2004001831 A2		HU 2004-1831	20021023
US 20040224980 A1		US 2004-832191	20040426
MX 2004004090 A1		MX 2004-4090	20040429

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1442021 A1	Based on	WO 2003037870 A
AU 2002346861 A1	Based on	WO 2003037870 A
HU 2004001831 A2	Based on	WO 2003037870 A
JP 2005511567 W	Based on	WO 2003037870 A
MX 2004004090 A1	Based on	WO 2003037870 A

PRIORITY APPLN. INFO: DE 2001-10153347 20011029
AN 2003-422751 [40] WPIX
AB DE 10153347 A1 UPAB: 20060119

NOVELTY - 3-substituted -1H-quinolin-2-one derivatives (I) and their tautomers, as diastereomers, enantiomers, racemic or other mixtures, bases, salts and solvates are new.

DETAILED DESCRIPTION - 3-substituted-1H-quinolin-2-one derivatives of formula (I) and their tautomers, as diastereomers, enantiomers, racemic or other mixtures, bases, salts and solvates are new.

R1-R4 = 1-10C linear or branched, saturated or unsaturated aliphatic group, (un)saturated 3-7C cycloaliphatic group, both optionally attached through an ether bridge, or is H, halo or hydroxy, or R3 and R4 together form a 5-7 membered ring;

R5 = H, 1-10C linear or branched, (un)saturated aliphatic group, aryl or heteroaryl;

R6 = hydroxy or OR7;

R7 = 1-10C linear or branched, saturated or unsaturated aliphatic group, or (un)saturated 3-6C cycloaliphatic group;

A' = (CH2)3, CH2-CH=CH, CH2COO, CH2CONH, (CH2)2O(CH2)pCO, (CH2)2O or (CH2)2NR1', all bound to X' through the right-hand end as written;

R1' = H, 1-10C linear or branched, (un)saturated aliphatic group, aryl or heteroaryl;

X' = one of many specified cycloaliphatic or heterocyclic groups; and

p = 0 or 1.

The full definitions are given in the Definitions Field (Full Definitions).

An INDEPENDENT CLAIM is also included for many methods for preparing (I).

ACTIVITY - Analgesic; Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Cerebroprotective; Vasotropic; Antiinflammatory; Neuroleptic; Anti-HIV; Antimigraine; Antiallergic; Antidepressant; Uropathic; Antidiarrheic; Antipruritic; Tranquilizer; Respiratory; Auditory; Dermatological.

The compound 2-(7-chloro-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)- N-(3-(N,N-dimethylaminomethyl)-4-hydroxy-4-(3-methoxyphenyl)cyclohexyl)acetamide, when administered intravenously at 10 mg/kg, gave 60% inhibition of phenylquinone-induced writhing in mice.

MECHANISM OF ACTION - None given.

USE - (I) are used, most particularly, to treat pain (chronic or neuropathic) and to treat or prevent neurodegeneration (Alzheimer's, Parkinson's or Huntington's diseases), stroke, cerebral ischemia or infarct, cerebral edema, inadequate provisioning of the central nervous system (hypoxia or anoxia), epilepsy, schizophrenia, psychosis associated with elevated amino acid levels, AIDS-related dementia, Tourette syndrome, encephalomyelitis, perinatal asphyxia, tinnitus, migraine, inflammatory and/or allergic reactions, depression, emotional disorders, urinary incontinence, itching and diarrhea. (I) are also used for anxiolysis and anesthesia.

L28 ANSWER 40 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-422750 [40] WPIX
DOC. NO. CPI: C2003-111617 [40]
TITLE: New quinoxalin-2-one derivatives, useful for treating e.g. chronic and neuropathic pain, neurodegenerative diseases, stroke, epilepsy, Tourette syndrome, schizophrenia, encephalomyelitis, diarrhea and depression
DERWENT CLASS: B02
INVENTOR: BUSCHMANN H; BUSCHMANN H H; ENGLBERGER W; ENGLBERGER W G; ENLGBERGER W; KOEGEL B; PRZEWOSNY M; SATTLEGGER M; SCHICK H
PATENT ASSIGNEE: (BUSC-I) BUSCHMANN H; (ENGL-I) ENGLBERGER W; (CHEF-C) GRUENENTHAL GMBH; (KOEG-I) KOEGEL B; (PRZE-I) PRZEWOSNY M; (SATT-I) SATTLEGGER M; (SCHI-I) SCHICK H
COUNTRY COUNT: 100

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10153345	A1	20030508	(200340)*	DE	25[0]	
WO 2003037879	A1	20030508	(200340)	DE		
EP 1444212	A1	20040811	(200452)	DE		
AU 2002350608	A1	20030512	(200464)	EN		
US 20040224954	A1	20041111	(200475)	EN		
HU 2004001829	A2	20050128	(200519)	HU		
JP 2005512986	W	20050512	(200532)	JA	77	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10153345 A1		DE 2001-10153345	20011029
AU 2002350608 A1		AU 2002-350608	20021023
EP 1444212 A1		EP 2002-785285	20021023
WO 2003037879 A1		WO 2002-EP11832	20021023
EP 1444212 A1		WO 2002-EP11832	20021023
US 20040224954 A1	Cont of	WO 2002-EP11832	20021023
HU 2004001829 A2		WO 2002-EP11832	20021023
JP 2005512986 W		WO 2002-EP11832	20021023
JP 2005512986 W		JP 2003-540161	20021023
HU 2004001829 A2		HU 2004-1829	20021023
US 20040224954 A1		US 2004-832205	20040426

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1444212 A1	Based on	WO 2003037879 A
AU 2002350608 A1	Based on	WO 2003037879 A
HU 2004001829 A2	Based on	WO 2003037879 A
JP 2005512986 W	Based on	WO 2003037879 A

PRIORITY APPLN. INFO: DE 2001-10153345 20011029
AN 2003-422750 [40] WPIX
AB DE 10153345 A1 UPAB: 20060119

NOVELTY - 3-substituted -1H-quinoxalin-2-one derivatives (I) and their tautomers, as diastereomers, enantiomers, racemic or other mixtures, bases, salts and solvates are new.

DETAILED DESCRIPTION - 3-substituted -1H-quinoxalin-2-one derivatives of formula (I) and their tautomers, as diastereomers, enantiomers, racemic or other mixtures, bases, salts and solvates are new.

R1-R4 = 1-10C linear or branched, saturated or unsaturated aliphatic group, (un)saturated 3-7C cycloaliphatic group, both optionally attached through an ether bridge, or is H, halo or hydroxy, or R3 and R4 together form a 5-7 membered ring;

A' = (CH2)n+2, (CH2)n-CH=CH, (CH2)n-COO, (CH2)nCONH, (CH2)n+1O(CH2)pCO, (CH2)n+1O, (CH2)n+1NR1' or NH(CH2)r, all bound to X through the right-hand end as written;

R1' = H, 1-10C linear or branched, (un)saturated aliphatic, 3-7C (un)saturated cycloaliphatic, aryl or heteroaryl residue;

X' = a specified cycloaliphatic or heterocyclic group;

n = 0-3;

p = 0 or 1; and

r = 0-2.

The full definitions are given in the Definitions Field (Full Definitions).

INDEPENDENT CLAIMS are also included for the following:

(1) Many methods for preparing (I);

(2) 4-substituted cyclohexane derivatives of formula (II); and

(3) Many methods for preparing (II).

RI = keto, aldehyde, NHR1, CO(CH2)p-OH, (CH2)r-OH or (CH2)r-Br;

Z' = phenyl, optionally containing at least one sulfur, oxygen or nitrogen as ring atom;

R2' = 1-10C linear or branched, (un)saturated aliphatic, 3-7C (un)saturated cycloaliphatic, aryl or heteroaryl residue, all optionally linked through (thio)ether or sulfonyl, or is H, halo, hydroxy, thiol, cyano or nitro, CH2F, CHF2, CF3 or N(R1')2; and

R3' = 1-10C linear or branched, (un)saturated aliphatic, 3-7C (un)saturated cycloaliphatic, aryl or heteroaryl residue, optionally linked through ether or ester, also H, halo or hydroxy.

ACTIVITY - Analgesic; Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Cerebroprotective; Vasotropic; Antiinflammatory; Neuroleptic; Anti-HIV; Antimigraine; Antiallergic; Antidepressant; Uropathic; Antidiarrheic; Antipruritic; Dermatological; Auditory; Respiratory; Tranquilizer.

The compound 6,7-dimethyl-3-oxo-3,4-dihydroquinoxalin-2-carboxylic acid 3-(N,N-dimethylaminomethyl)-4-hydroxy-4-(3- methoxyphenyl)cyclohexylamide, when administered intravenously at 10 mg/kg, gave 72% inhibition of phenylquinone-induced writhing in mice.

MECHANISM OF ACTION - None given.

USE - (I) are used most particularly, to treat pain (chronic or neuropathic) and to treat or prevent neurodegeneration (Alzheimer's, Parkinson's or Huntington's diseases), stroke, cerebral ischemia or infarct,

cerebral edema, inadequate provisioning of the central nervous system (hypoxia or anoxia), epilepsy, schizophrenia, psychosis associated with elevated amino acid levels, AIDS-related dementia, Tourette syndrome, encephalomyelitis, perinatal asphyxia, tinnitus, migraine, inflammatory and/or allergic reactions, depression, emotional disorders, urinary incontinence, itching and diarrhea. (I) are also useful as anxiolytics and anesthetics.

L28 ANSWER 41 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-120521 [11] WPIX
CROSS REFERENCE: 2003-111937; 2003-148331
DOC. NO. CPI: C2003-031106 [11]
TITLE: New 1-(pyridin-2-yl)-cyclohexane-1,4-diamine derivatives, are opioid receptor-like 1 receptor ligands useful e.g. for treating pain, anxiety, stress, depression, epilepsy or cognitive, learning and memory deficiency
DERWENT CLASS: B02; B03
INVENTOR: BUSCHMANN H; HELLER B; MAUL C; SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 99

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002090330	A1	20021114	(200311)*	DE	72[0]	
NO 2003004931	A	20040102	(200409)	NO		
EP 1385825	A1	20040204	(200410)	DE		
SK 2003001378	A3	20040406	(200427)	SK		
CZ 2003002995	A3	20040218	(200430)	CS		
BR 2002009579	A	20040622	(200442)	PT		
US 20040147741	A1	20040729	(200450)	EN		
AU 2002341195	A1	20021118	(200452)	EN		
JP 2004528374	W	20040916	(200461)	JA	113	
HU 2004000989	A2	20040830	(200465)	HU		
NZ 529334	A	20041029	(200474)	EN		
ZA 2003009521	A	20041124	(200481)	EN	87	
MX 2003010201	A1	20060201	(200649)	ES		
RU 2287523	C2	20061120	(200677)	RU		
AU 2002341195	B2	20070104	(200731)	EN		
EP 1385825	B1	20070815	(200755)	DE		
DE 50210707	G	20070927	(200765)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002090330	A1	WO 2002-EP5078	20020508
AU 2002341195	A1	AU 2002-341195	20020508
AU 2002341195	B2	AU 2002-341195	20020508
BR 2002009579	A	BR 2002-9579	20020508
EP 1385825	A1	EP 2002-750900	20020508
EP 1385825	B1	EP 2002-750900	20020508
JP 2004528374	W	JP 2002-587410	20020508
NZ 529334	A	NZ 2002-529334	20020508
NO 2003004931	A	WO 2002-EP5078	20020508
EP 1385825	A1	WO 2002-EP5078	20020508
SK 2003001378	A3	WO 2002-EP5078	20020508
CZ 2003002995	A3	WO 2002-EP5078	20020508
BR 2002009579	A	WO 2002-EP5078	20020508

US 20040147741 A1 Cont of	WO 2002-EP5078 20020508
JP 2004528374 W	WO 2002-EP5078 20020508
HU 2004000989 A2	WO 2002-EP5078 20020508
NZ 529334 A	WO 2002-EP5078 20020508
MX 2003010201 A1	WO 2002-EP5078 20020508
RU 2287523 C2	WO 2002-EP5078 20020508
EP 1385825 B1	WO 2002-EP5078 20020508
MX 2003010201 A1	MX 2003-10201 19990409
CZ 2003002995 A3	CZ 2003-2995 20020508
RU 2287523 C2	RU 2003-134145 20020508
SK 2003001378 A3	SK 2003-1378 20020508
NO 2003004931 A	NO 2003-4931 20031105
US 20040147741 A1	US 2003-704200 20031110
ZA 2003009521 A	ZA 2003-9521 20031208
HU 2004000989 A2	HU 2004-989 20020508
DE 50210707 G	DE 2002-510707 20020508
DE 50210707 G	EP 2002-750900 20020508
DE 50210707 G	WO 2002-EP5078 20020508

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1385825	A1	Based on	WO 2002090330	A
SK 2003001378	A3	Based on	WO 2002090330	A
CZ 2003002995	A3	Based on	WO 2002090330	A
BR 2002009579	A	Based on	WO 2002090330	A
AU 2002341195	A1	Based on	WO 2002090330	A
JP 2004528374	W	Based on	WO 2002090330	A
HU 2004000989	A2	Based on	WO 2002090330	A
NZ 529334	A	Based on	WO 2002090330	A
MX 2003010201	A1	Based on	WO 2002090330	A
RU 2287523	C2	Based on	WO 2002090330	A
AU 2002341195	B2	Based on	WO 2002090330	A
EP 1385825	B1	Based on	WO 2002090330	A
DE 50210707	G	Based on	EP 1385825	A
DE 50210707	G	Based on	WO 2002090330	A

PRIORITY APPLN. INFO: DE 2001-10123163 20010509
AN 2003-120521 [11] WPIX
CR 2003-111937; 2003-148331
AB WO 2002090330 A1 UPAB: 20060118
NOVELTY - Substituted 1-(pyridin-2-yl)-cyclohexane-1,4-diamine derivatives (I) are new.

DETAILED DESCRIPTION - Cyclohexane derivatives of formula (I), including their racemates, pure stereoisomers (especially enantiomers or diastereomers), stereoisomer mixtures, salts and solvates (specifically hydrates), are new.

R1, R2 = H; or Alk, Cyc, Ar, Het, -A-Ar, -A-Cyc' or -A-Het (all optionally substituted (os));

or NR1R2 = morpholino, N-(R6)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;

Alk = optionally unsaturated 1-8C alkyl;

Cyc = optionally unsaturated 3-8C cycloalkyl;

Ar = aryl;

Het = heteroaryl;

A = 1-3C alkylene;

Cyc' = 3-8C cycloalkyl;

R6 = H; or Alk, Cyc, Ar, Het, -A-Ar, -A-Cyc' or -A-Het (all os);

R3 = as R6; or SH, OH, halo, CN, NO2, OR26 or NR27R28;

R26 = Alk' or Cyc (both os); or Ar, Het, -A'-Ar, -A'-Cyc' or -A'-Het (all os by one or more of halo, NH2, NO2, CF3, CHF2, CH2F, 1-4C alkyl, OCF3, OCHF2, OCH2F, 1-4C alkoxy, SH and/or OH);

A' = optionally unsaturated 1-3C alkylene;

Alk' = optionally unsaturated 1-6C alkyl;

R27, R28 = H or as R26;

or NR27R28 = morpholino, N-(R29)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;

R29 = H or as R26;

R4 = H, os Alk, C(X)R7, C(X)NR7R8, C(X)XR9 or SO2R9;

X = O or S;

R7 = H; or Alk, Cyc, -A''-Ar, -A''-Cyc or -A''-Het (all os);

A'' = os, optionally unsaturated 1-4C alkylene;

R8 = H or os, optionally unsaturated 1-4C alkyl;

or NR7R8 = morpholino, N-(R10)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;

R10 = as R6;

R9 = as R7, but not H;

R5 = Cyc', Ar or Het (all os); or -CHR11(CH2)nR12 or -C(Y)(CH2)nR12;

or NR4R5 = os, saturated or unsaturated 3-8 membered heterocycle (optionally fused with further rings);

Y = O, S or H2;

n = 0-3;

R11 = H, optionally unsaturated, os 1-7C alkyl or optionally unsaturated (1-6C) alkoxycarbonyl;

R12 = H; or Cyc', Ar or Het (all os).

INDEPENDENT CLAIMS are also included for:

(1) The preparation of (I); and

(2) (I) containing medicaments and also optionally containing an opioid (preferably a strong opioid, especially morphine) or an anesthetic (preferably hexobarbital or halothane).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Nootropic; Neuroprotective; Vasotropic; Cardiant; Hypotensive; Hypertensive; Antipruritic; Antimigraine; Laxative; Anorectic; Antidiarrheic;

Immunomodulator; Uropathic; Relaxant; Anesthetic; Diuretic. In the mouse tail-flick analgesic test, the non-polar diastereomer of N'-(2-(1H-indol-3-yl)-ethyl)-N,N-dimethyl-1-pyridin-2-yl-cyclohexane-1,4- diamine trihydrochloride (Ia) at 10 mg/kg i.v. gave 91% of the maximum possible analgesic activity.

MECHANISM OF ACTION - ORL1 (opioid receptor-like) receptor ligand; nociceptin/ORL1 receptor system mediator. (Ia) had Ki 0.093 microM in an ORL1 binding assay.

USE - (I) are used for treating pain (especially acute neuropathic or chronic pain), anxiety, stress (and associated symptoms), depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory problems, withdrawal symptoms, drug and/or alcohol abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, gastric motility problems, eating disorders, anorexia, fatty degeneration, locomotion disorders, diarrhea, cachexia or urinary incontinence; as muscle relaxants, anticonvulsants or anesthetics or for co-adminstration with an opioid analgesic or anesthetic, for diuresis, antinatriuresis and/or anxiolysis (all claimed).

ADVANTAGE - (I) have strong ORL1 receptor binding activity.

L28 ANSWER 42 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-699532 [76] WPIX
DOC. NO. CPI: C2002-198328 [76]
TITLE: Medicaments, useful for treating pain, urinary

incontinence, pruritis, tinnitus or diarrhea, especially severe pain, comprise new or known substituted propane-1,3-diamine derivatives

DERWENT CLASS: B05

INVENTOR: BUSCHMANN H; KOEGEL B; KOGEL B; KOGEL B Y; MERLA B; RISCH N; SUNDERMANN B

PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH

COUNTRY COUNT: 99

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10108307	A1	20020829	(200276)*	DE	38[0]	
WO 2002066432	A1	20020829	(200276)	DE		
CZ 2003001968	A3	20031015	(200374)	CS		
NO 2003003697	A	20031017	(200375)	NO		
EP 1363885	A1	20031126	(200380)	DE		
HU 2003002746	A2	20031229	(200413)	HU		
SK 2003001030	A3	20040108	(200413)	SK		
BR 2002007535	A	20040309	(200420)	PT		
KR 2003091995	A	20031203	(200424)	KO		
US 20040067928	A1	20040408	(200426)	EN		
AU 2002246095	A1	20020904	(200427)	EN		
MX 2003006744	A1	20031201	(200470)	ES		
JP 2005503330	W	20050203	(200516)	JA	153	
ZA 2003007321	A	20050330	(200527)	EN	111	
CN 1610668	A	20050427	(200558)	ZH		
EP 1363885	B1	20070523	(200735)	DE		
US 7230018	B2	20070612	(200740)	EN		
DE 50210197	G	20070705	(200744)	DE		
AU 2002246095	B2	20070628	(200765)	EN		
ES 2286240	T3	20071201	(200782)	ES		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10108307 A1		DE 2001-10108307	20010221
AU 2002246095 A1		AU 2002-246095	20020220
AU 2002246095 B2		AU 2002-246095	20020220
BR 2002007535 A		BR 2002-7535	20020220
CN 1610668 A		CN 2002-805246	20020220
DE 50210197 G		DE 2002-510197	20020220
EP 1363885 A1		EP 2002-714169	20020220
EP 1363885 B1		EP 2002-714169	20020220
DE 50210197 G		EP 2002-714169	20020220
JP 2005503330 W		JP 2002-565949	20020220
WO 2002066432 A1		WO 2002-EP1765	20020220
CZ 2003001968 A3		WO 2002-EP1765	20020220
NO 2003003697 A		WO 2002-EP1765	20020220
EP 1363885 A1		WO 2002-EP1765	20020220
SK 2003001030 A3		WO 2002-EP1765	20020220
HU 2003002746 A2		WO 2002-EP1765	20020220
BR 2002007535 A		WO 2002-EP1765	20020220
US 20040067928 A1	Cont of	WO 2002-EP1765	20020220
MX 2003006744 A1		WO 2002-EP1765	20020220
JP 2005503330 W		WO 2002-EP1765	20020220
EP 1363885 B1		WO 2002-EP1765	20020220
US 7230018 B2	Cont of	WO 2002-EP1765	20020220

DE 50210197 G	WO 2002-EP1765 20020220
CZ 2003001968 A3	CZ 2003-1968 20020220
HU 2003002746 A2	HU 2003-2746 20020220
SK 2003001030 A3	SK 2003-1030 20020220
MX 2003006744 A1	MX 2003-6744 20030729
NO 2003003697 A	NO 2003-3697 20030820
KR 2003091995 A	KR 2003-711008 20030821
US 20040067928 A1	US 2003-644981 20030821
US 7230018 B2	US 2003-644981 20030821
ZA 2003007321 A	ZA 2003-7321 20030918
ES 2286240 T3	EP 2002-714169 20020220

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
DE 50210197	G	Based on	EP 1363885	A
CZ 2003001968	A3	Based on	WO 2002066432	A
EP 1363885	A1	Based on	WO 2002066432	A
SK 2003001030	A3	Based on	WO 2002066432	A
HU 2003002746	A2	Based on	WO 2002066432	A
BR 2002007535	A	Based on	WO 2002066432	A
AU 2002246095	A1	Based on	WO 2002066432	A
MX 2003006744	A1	Based on	WO 2002066432	A
JP 2005503330	W	Based on	WO 2002066432	A
EP 1363885	B1	Based on	WO 2002066432	A
DE 50210197	G	Based on	WO 2002066432	A
AU 2002246095	B2	Based on	WO 2002066432	A
ES 2286240	T3	Based on	EP 1363885	A

PRIORITY APPLN. INFO: DE 2001-10108307 20010221
AN 2002-699532 [76] WPIX
AB DE 10108307 A1 UPAB: 20060120
NOVELTY - Medicaments, comprising substituted propane-1,3-diamine derivatives (I), are new.

DETAILED DESCRIPTION - Medicaments, comprising propanediamine derivatives of formula (I) or their salts, in the form of racemate, one or more diastereomers or one or more enantiomers, are new.

R1 = 1-12C alkyl, cycloalkyl, cycloalkylalkyl or aryl;

R2 = 1-12C alkyl, cycloalkyl, aryl, cycloalkylalkyl, aralkyl, heterocyclyl or heterocyclylalkyl; or

R1 + R2 = (CH2)m (ring being optionally substituted by one or more of alkyl, alkoxy or aralkoxy or benzo-fused);

m = 2-6;

R3 = H, 1-12C alkyl, cycloalkyl, aryl, cycloalkylalkyl, aralkyl, heterocyclyl, heterocyclylalkyl or -CO-R7;

R4 = H, 1-12C alkyl, cycloalkyl, aryl, cycloalkylalkyl, aralkyl, heterocyclyl or heterocyclylalkyl; or

R3 + R4 = (CH2)n or (CH2)2-X-(CH2)2 (both optionally substituted by alkyl);

n = 3-7;

X = O, S or NR8;

R5, R6 = 1-12C alkyl, cycloalkyl, aryl, cycloalkylalkyl or aralkyl; or

R5 + R6 = (CH2)n or (CH2)2-X-(CH2)2 (both optionally substituted by alkyl); or

R3 + R4 = (CH2)n or (CH2)2-X-(CH2)2 (both optionally substituted by alkyl);

X = O, S or NR8;

A = aryl, heteroaryl, COOR10 or 2-propyl;

R7 = alkyl, cycloalkyl, aryl, heterocyclyl, cycloalkylalkyl, aralkyl or heterocyclylalkyl;

R8, R9 = H, alkyl, cycloalkyl, aryl, cycloalkylalkyl, aralkyl or heterocyclyl; and

R10 = alkyl, cycloalkyl, aryl, cycloalkylalkyl or aralkyl.

Provided that R1 and R2 are not at the same time aryl or aryl and heterocyclyl.

Unless specified otherwise alkyl moieties have 1-6C and cycloalkyl moieties 3-8C.

INDEPENDENT CLAIMS are included for:

(1) (I) and their salts as new compounds, with the exception of N,N-dimethyl-(phenyl-(2-pyrrolidin-1-yl-cyclohexyl)-methyl)-amine, N,N-dimethyl-(phenyl-(2-morpholin-1-yl-cyclohexyl)-methyl)-amine, 4-(phenyl-(2-pyrrolidin-1-yl-cyclohexyl)-methyl)-pyrrolidine, 4-(phenyl-(2-pyrrolidin-1-yl-cyclohexyl)-methyl)-morpholine, 1-(phenyl-(2-pyrrolidin-1-yl-cyclohexyl)-methyl)-piperidine, 1-(2-methyl-(2-pyrrolidin-1-yl-cyclohexyl)-propyl)-piperidine, N,N-dimethyl-(2-methyl-1,3-diphenyl-3-pyrrolidin-1-yl-propyl)-methyl)- amine, N,N-dimethyl-(2-methyl-1,3-diphenyl-3-(N,N-diethylamino)-propyl)- methyl)-amine, 4-(1,3-diphenyl-3-pyrrolidin-1-yl-propyl)-morpholine, N,N-dimethyl-(2-methyl-1-phenyl-3-(morpholin-4-yl-propyl)-pentyl)-amine, benzyl-(2-(dimethylamino-phenyl-methyl)-cyclohexyl)-amine and (2-methyl-1,3-diphenyl-3-piperidin-1-yl-propyl)-propylamine; and

(2) Preparation of (I).

ACTIVITY - Analgesic; Uropathic; Antipruritic; Auditory; Antidiarrheic.

In the phenylquinone-induced mouse writhing test for analgesic activity, (syn, syn)-2-chloro-N-(2-(dimethylaminopyridin-3-ylmethyl)-cyclohexyl)-benzamide (Ia) (as the hydrochloride) inhibited writhing reaction by 85% at a dose of 10 mg/kg i.v.

MECHANISM OF ACTION - None given in the source material.

USE - (I) are used for treating and/or preventing pain, urinary incontinence, pruritis, tinnitus or diarrhea (all claimed). (I) are especially used for treating and/or preventing acute, chronic or neuropathic pain, particularly severe to very severe pain.

ADVANTAGE - (I) are free of the side-effects (e.g. nausea, emesis, dependence, respiratory suppression and constipation) of conventional opioid analgesics such as morphine.

L28 ANSWER 43 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-394463 [42] WPIX
DOC. NO. CPI: C2002-111092 [42]
TITLE: New cyclohexylmethyl-amine derivatives, useful as analgesics for treating neuropathic and chronic pain
DERWENT CLASS: B05
INVENTOR: BERNARD S; BUSCHMANN H; BUSCHMANN H H; DE ESPLUGUES L; FINKAM M; KOEGEL B; KOEGEL B Y; KOGEL B; MAUL C; MUCHAEL F; SUNDERMANN B; SUNDERMANN C
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 96

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002030870	A2	20020418	(200242)*	DE	153[0]	
DE 10049481	A1	20020502	(200242)	DE		
AU 2002013978	A	20020422	(200254)	EN		
NO 2003001386	A	20030526	(200346)	NO		
CZ 2003000906	A3	20030618	(200347)	CS		
SK 2003000341	A3	20030805	(200360)	SK		

KR 2003059165	A	20030707 (200377)	KO	
EP 1368299	A2	20031210 (200382)	DE	
US 20030232891	A1	20031218 (200401)	EN	
HU 2003003184	A2	20031229 (200413)	HU	
MX 2003002348	A1	20030701 (200420)	ES	
JP 2004524274	W	20040812 (200453)	JA	292
ZA 2003003224	A	20041027 (200474)	EN	186
BR 2001014379	A	20041214 (200510)	PT	
CN 1547570	A	20041117 (200516)	ZH	
EP 1571140	A1	20050907 (200559)	DE	
EP 1368299	B1	20060726 (200650)	DE	
NZ 525170	A	20060831 (200659)	EN	
DE 50110569	G	20060907 (200660)	DE	
ES 2267833	T3	20070316 (200722)	ES	
RU 2295515	C2	20070320 (200752)	RU	
NZ 545879	A	20070831 (200763)	EN	
US 7273952	B2	20070925 (200765)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002030870	A2	WO 2001-EP11246	20010928
DE 10049481	A1	DE 2000-10049481	20000929
BR 2001014379	A	BR 2001-14379	20010928
CN 1547570	A	CN 2001-816495	20010928
DE 50110569	G	DE 2001-510569	20010928
EP 1368299	A2	EP 2001-982379	20010928
EP 1571140	A1 Div Ex	EP 2001-982379	20010928
EP 1368299	B1	EP 2001-982379	20010928
DE 50110569	G	EP 2001-982379	20010928
ES 2267833	T3	EP 2001-982379	20010928
NZ 545879	A Div Ex	NZ 2001-280901	20010928
NZ 525170	A	NZ 2001-525170	20010928
NZ 545879	A	NZ 2001-545879	20010928
NO 2003001386	A	WO 2001-EP11246	20010928
CZ 2003000906	A3	WO 2001-EP11246	20010928
SK 2003000341	A3	WO 2001-EP11246	20010928
EP 1368299	A2	WO 2001-EP11246	20010928
US 20030232891	A1 Cont of	WO 2001-EP11246	20010928
HU 2003003184	A2	WO 2001-EP11246	20010928
MX 2003002348	A1	WO 2001-EP11246	20010928
JP 2004524274	W	WO 2001-EP11246	20010928
BR 2001014379	A	WO 2001-EP11246	20010928
EP 1368299	B1	WO 2001-EP11246	20010928
NZ 525170	A	WO 2001-EP11246	20010928
DE 50110569	G	WO 2001-EP11246	20010928
RU 2295515	C2	WO 2001-EP11246	20010928
AU 2002013978	A	AU 2002-13978	20010928
JP 2004524274	W	JP 2002-534259	20010928
CZ 2003000906	A3	CZ 2003-906	20010928
HU 2003003184	A2	HU 2003-3184	20010928
RU 2295515	C2	RU 2003-111757	20010928
SK 2003000341	A3	SK 2003-341	20010928
MX 2003002348	A1	MX 2003-2348	20030318
NO 2003001386	A	NO 2003-1386	20030326
KR 2003059165	A	KR 2003-704578	20030329
US 20030232891	A1	US 2003-402260	20030331
ZA 2003003224	A	ZA 2003-3224	20030424
EP 1571140	A1	EP 2005-11581	20010928

EP 1368299 B1 Related to EP 2005-11581 20050530
US 7273952 B2 Cont of WO 2001-EP11246 20010928
US 7273952 B2 US 2003-402260 20030331

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1571140	A1	Div ex	EP 1368299	A
DE 50110569	G	Based on	EP 1368299	A
ES 2267833	T3	Based on	EP 1368299	A
EP 1368299	B1	Related to	EP 1571140	A
AU 2002013978	A	Based on	WO 2002030870	A
CZ 2003000906	A3	Based on	WO 2002030870	A
SK 2003000341	A3	Based on	WO 2002030870	A
EP 1368299	A2	Based on	WO 2002030870	A
HU 2003003184	A2	Based on	WO 2002030870	A
MX 2003002348	A1	Based on	WO 2002030870	A
JP 2004524274	W	Based on	WO 2002030870	A
BR 2001014379	A	Based on	WO 2002030870	A
EP 1368299	B1	Based on	WO 2002030870	A
NZ 525170	A	Based on	WO 2002030870	A
DE 50110569	G	Based on	WO 2002030870	A
RU 2295515	C2	Based on	WO 2002030870	A
NZ 545879	A	Div ex	NZ 525170	A

PRIORITY APPLN. INFO: DE 2000-10049481 20000929
AN 2002-394463 [42] WPIX
AB WO 2002030870 A2 UPAB: 20060119

NOVELTY - Substituted cyclohexylmethyl-amine derivatives (I), optionally as racemates, pure or mixed stereoisomers (especially enantiomers and diastereomers), salts with acids or bases and/or solvates, especially hydrates.

DETAILED DESCRIPTION - Substituted cyclohexylmethyl-amine derivatives of formula (I), optionally as racemates, pure or mixed stereoisomers (especially enantiomers and diastereomers), salts with acids or bases and/or solvates, especially hydrates are new

A = hydrogen or (hetero)aryl, optionally substituted one or more times;

R1 = 1-10C alkyl or 3-10C cycloalkyl, optionally unsaturated, linear or branched and substituted one or more times; (hetero)aryl, or (hetero)aryl or 3-10C cycloalkyl connected through 1-3C alkyl (optionally unsaturated), 1-3C alkylene or ethynyl, all optionally substituted one or more times by fluoro, chloro, bromo, iodo, OR18, SR18, SO2R18, SO2OR18, cyano, COOR18, NR19R20, 1-10C alkyl, 3-10C cycloalkyl or silyl (optionally substituted one or more times), (hetero)aryl (optionally substituted one or more times), or (hetero)aryl or 3-10C cycloalkyl, connected through 1-3C alkyl (optionally unsaturated) or 1-3C alkylene;

R18, R19 and R20 = hydrogen, 1-10C alkyl or 3-10C cycloalkyl, optionally unsaturated, linear or branched and substituted one or more times; (hetero)aryl, or (hetero)aryl or 3-10C cycloalkyl connected through 1-3C alkyl (optionally unsaturated) or 1-3C alkylene, or R19 and R20 are together CH2CH2(O or R21)CH2CH2, or (CH2)z;

z = 3-6;

R21 = hydrogen, optionally substituted phenyl or 1-10C alkyl, saturated or unsaturated, linear or branched, optionally substituted one or more times;

R2 and R3 = as defined for R18, or together form a ring as for R19 and R20;

X completes one of the partial structures B = hydroxy, OR7, hydrogen, fluoro, chloro or NR8R9; R7 = R18 but not hydrogen; R8 and R9 are as R18 or

together form a ring as R19 and R20; Z-Y = any of five specified groups; some compounds are excluded by provisos
. The full definitions are given in the DEFINITIONS (Full Definitions) Field.
ACTIVITY - Analgesic. No details of tests for analgesic activity are given.
MECHANISM OF ACTION - None given in the source material.
USE - (I) are used to treat pain, specifically neuropathic or chronic pain.

L28 ANSWER 44 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-523229 [58] WPIX
DOC. NO. CPI: C2001-156383 [58]
TITLE: New 3-phenyl-4-aminomethyl-cyclohexanone derivatives, useful e.g. for treating inflammation, allergy or, especially, pain
DERWENT CLASS: B05
INVENTOR: BUSCHMANN H; KOEGEL B; KOGEL B; KOGEL B Y; PUETZ C; PUETZ C K; PUTZ C
PATENT ASSIGNEE: (BUSC-I) BUSCHMANN H; (CHEF-C) GRUENENTHAL GMBH; (KOEG-I) KOEGEL B; (PUET-I) PUETZ C
COUNTRY COUNT: 93

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10000311	A1	20010712	(200158)*	DE	27[0]	
WO 2001049651	A2	20010712	(200158)	DE		
AU 2001030169	A	20010716	(200169)	EN		
EP 1246791	A2	20021009	(200267)	DE		
NO 2002002983	A	20020828	(200270)	NO		
CZ 2002002338	A3	20021113	(200282)	CS		
KR 2002063296	A	20020801	(200308)	KO		
BR 2000016941	A	20030225	(200320)	PT		
SK 2002000980	A3	20030304	(200321)	SK		
HU 2002003859	A2	20030328	(200333)	HU		
US 20030096811	A1	20030522	(200336)	EN		
JP 2003519209	W	20030617	(200349)	JA	82	
MX 2002006697	A1	20021001	(200370)	ES		
CN 1437575	A	20030820	(200374)	ZH		
NZ 520468	A	20031128	(200382)	EN		
ZA 2002006150	A	20040128	(200420)	EN	105	
EP 1246791	B1	20041027	(200471)	DE		
DE 50008447	G	20041202	(200479)	DE		
US 6890959	B2	20050510	(200532)	EN		
ES 2231304	T3	20050516	(200535)	ES		
AU 782862	B2	20050901	(200565)	EN		
MX 235008	B	20060317	(200651)	ES		
IL 150558	A	20070308	(200726)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10000311 A1		DE 2000-10000311	20000105
BR 2000016941 A		BR 2000-16941	20001227
CN 1437575 A		CN 2000-819266	20001227
DE 50008447 G		DE 2000-508447	20001227

EP 1246791 A2	EP 2000-990824 20001227
EP 1246791 B1	EP 2000-990824 20001227
DE 50008447 G	EP 2000-990824 20001227
ES 2231304 T3	EP 2000-990824 20001227
NZ 520468 A	NZ 2000-520468 20001227
WO 2001049651 A2	WO 2000-EP13282 20001227
EP 1246791 A2	WO 2000-EP13282 20001227
NO 2002002983 A	WO 2000-EP13282 20001227
CZ 2002002338 A3	WO 2000-EP13282 20001227
BR 2000016941 A	WO 2000-EP13282 20001227
SK 2002000980 A3	WO 2000-EP13282 20001227
HU 2002003859 A2	WO 2000-EP13282 20001227
US 20030096811 A1 Cont of	WO 2000-EP13282 20001227
JP 2003519209 W	WO 2000-EP13282 20001227
MX 2002006697 A1	WO 2000-EP13282 20001227
NZ 520468 A	WO 2000-EP13282 20001227
EP 1246791 B1	WO 2000-EP13282 20001227
DE 50008447 G	WO 2000-EP13282 20001227
US 6890959 B2 Cont of	WO 2000-EP13282 20001227
MX 235008 B	WO 2000-EP13282 20001227
AU 2001030169 A	AU 2001-30169 20001227
AU 782862 B2	AU 2001-30169 20001227
JP 2003519209 W	JP 2001-550191 20001227
CZ 2002002338 A3	CZ 2002-2338 20001227
HU 2002003859 A2	HU 2002-3859 20001227
SK 2002000980 A3	SK 2002-980 20001227
NO 2002002983 A	NO 2002-2983 20020620
KR 2002063296 A	KR 2002-708706 20020704
MX 2002006697 A1	MX 2002-6697 20020705
MX 235008 B	MX 2002-6697 20020705
US 20030096811 A1	US 2002-189184 20020705
US 6890959 B2	US 2002-189184 20020705
ZA 2002006150 A	ZA 2002-6150 20020801
IL 150558 A	IL 2000-150558 20001227

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 782862	B2	Previous Publ	AU 2001030169	A
DE 50008447	G	Based on	EP 1246791	A
ES 2231304	T3	Based on	EP 1246791	A
AU 2001030169	A	Based on	WO 2001049651	A
EP 1246791	A2	Based on	WO 2001049651	A
CZ 2002002338	A3	Based on	WO 2001049651	A
BR 2000016941	A	Based on	WO 2001049651	A
SK 2002000980	A3	Based on	WO 2001049651	A
HU 2002003859	A2	Based on	WO 2001049651	A
JP 2003519209	W	Based on	WO 2001049651	A
MX 2002006697	A1	Based on	WO 2001049651	A
NZ 520468	A	Based on	WO 2001049651	A
EP 1246791	B1	Based on	WO 2001049651	A
DE 50008447	G	Based on	WO 2001049651	A
AU 782862	B2	Based on	WO 2001049651	A
MX 235008	B	Based on	WO 2001049651	A
IL 150558	A	Based on	WO 2001049651	A

PRIORITY APPLN. INFO: DE 2000-10000311 20000105
AN 2001-523229 [58] WPIX
AB DE 10000311 A1 UPAB: 20060117

NOVELTY - 3-Phenyl-4-aminomethyl-cyclohexanone derivatives (A).

DETAILED DESCRIPTION - 3-Phenyl-4-aminomethyl-cyclohexanone derivatives (A), of formulae (I) and (Ia), their diastereomers and enantiomers, in free form or as acid-addition salts (especially hydrochlorides) are new:

R1 and R2 = R5 or Y'R5;

Y' = 1-10C alkyl or 2-10C alkenyl or alkynyl, linear or branched and optionally substituted one or more times;

R5 = hydrogen, fluoro, chloro, bromo, iodo, cyano, nitro, 1-8C alkyl, 2-8C alkenyl or alkynyl, linear or branched and optionally substituted one or more times, 3-7C cycloalkyl, saturated or unsaturated, optionally substituted one or more times, or the corresponding heterocycle with one ring C replaced by sulfur, oxygen or NR6;

R6 = hydrogen, 1-10C alkyl or 2-10C alkenyl or alkynyl, linear or branched and optionally substituted one or more times, or (hetero)aryl, optionally substituted one or more times; or OR7, OCOR7, OCOOR7, OCSR7, COR7, COOR7, CSR7, SR7, SOR7 or SO2R7;

R7 = hydrogen, 1-18C alkyl, 2-18C alkenyl or alkynyl, linear or branched and optionally substituted one or more times, 3-7C cycloalkyl, saturated or unsaturated, optionally substituted one or more times, or the corresponding heterocycle with one ring C replaced by sulfur, oxygen or NR8;

R8 = hydrogen, 1-10C alkyl or 2-10C alkenyl or alkynyl, linear or branched and optionally substituted one or more times, alkylaryl or (hetero)aryl, optionally substituted one or more times, NR9R10, CONR9R10 or SO2NR9R10;

R9 and R10 = R7, or together they form a 3-7C cycloalkyl, saturated or unsaturated, optionally substituted one or more times, or the corresponding heterocycle with one ring C replaced by sulfur, oxygen or NR12;

R12 = hydrogen, 1-10C alkyl or 2-10C alkenyl or alkynyl, linear or branched and optionally substituted one or more times;

together R1 and R2 may = -CH=CH-CH=CH-, forming a naphthyl ring, optionally substituted one or more times;

X = hydrogen, fluoro, chloro, bromo, iodo, tosyloxy, OR13 or OCOR13;

R13 = hydrogen, 1-10C alkyl or 2-10C alkenyl or alkynyl, linear or branched and optionally substituted, 3-7C cycloalkyl, saturated or unsaturated, optionally substituted one or more times, or the corresponding heterocycle with one ring C replaced by sulfur, oxygen or nitrogen, also alkylaryl or (hetero)aryl, optionally substituted one or more times; if X is absent a 2,3- or 3,4-double bond is present in the ring (formula (Ia)); and

R3 and R4 = R13, or together are as R9 and R10.

With the following provisos:

(1) where X = hydroxy, R2 = hydrogen, R3 and R4 = Me, then R1 is not OR7 (with R7 = hydrogen, Me or optionally substituted pyridyl, thienyl, thiazolyl or phenyl), OCOOR7 (with R7 = 1-5C alkyl,) or OCOR7 (with R7 = 1-5C alkyl, 1-3C alkylphenylamino, 2-3C alkoxycarbonyloxyphenyl, di(1-4C alkylamino)methylphenyl, N-morpholinomethylphenyl, or CHZ'-NHZ'', with Z' and Z'' = hydrogen or 1-6C alkyl); or

(2) when X = hydrogen or formula (Ia) with 2,3-double bond, R2 = hydrogen, R3 and R4 = 1-6C alkyl, aryl or 3-7C cycloalkyl, then R1 is not hydrogen, 1-6C alkoxy, 3-7C cycloalkoxy, aryloxy or heterocyclyloxy.

INDEPENDENT CLAIMS are also included for the following:

(a) methods for preparation of (I) and (Ia); and

(b) pharmaceutical composition containing (I) or (Ia).

ACTIVITY - Analgesic; antiallergic; antiinflammatory; antidepressant; antiaddictive; neurological; gastro-intestinal; cardiovascular; respiratory; psychological; antiepileptic; urogenital; antipruritic; antitussive; antidiarrhea.

In the standard phenylquinone-induced writhing test in mice, a 10 mg/kg intravenous dose of rac-cis-(4-dimethylaminomethyl-3-(3- methoxyphenyl)-cyclohexanone) hydrochloride caused a 96 % reduction in the writhing response.

MECHANISM OF ACTION - None given in the source material.

USE - (A) are especially useful for treatment of pain but may also be used to treat inflammatory and allergic reactions; depression; drug and alcohol misuse; gastritis; cardiovascular and respiratory diseases; coughs; psychological disorders and epilepsy, particularly urinary incontinence, pruritis and/or diarrhea.

L28 ANSWER 45 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-503416 [56] WPIX
DOC. NO. CPI: C2001-151469 [56]
TITLE: New 4-alkylidene-1-aminomethyl-2-phenyl-cyclohexane derivatives, useful e.g. for treating inflammation, allergy, depression, diarrhea, coughing, epilepsy or especially pain
DERWENT CLASS: B05
INVENTOR: KOEGEL B; KOGEL B; KOGEL B Y; PUETZ C; PUETZ C K; PUTZ C; STRASS-BURGER W; STRASSBURGER W; STRASSBURGER W W A
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH; (KOEG-I) KOEGEL B; (PUET-I) PUETZ C; (STRA-I) STRASSBURGER W
COUNTRY COUNT: 93

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
DE 10000312	A1	20010712	(200156)*	DE	42[0]	
WO 2001049654	A2	20010712	(200156)	DE		
AU 2001028438	A	20010716	(200169)	EN		
EP 1246793	A2	20021009	(200267)	DE		
NO 2002002985	A	20020828	(200270)	NO		
CZ 2002002337	A3	20021113	(200282)	CS		
KR 2002063294	A	20020801	(200308)	KO		
SK 2002000981	A3	20030204	(200318)	SK		
US 20030069288	A1	20030410	(200327)	EN		
BR 2000016942	A	20030610	(200341)	PT		
JP 2003519210	W	20030617	(200349)	JA	120	
MX 2002006700	A1	20021001	(200370)	ES		
CN 1437576	A	20030820	(200374)	ZH		
HU 2002004001	A2	20031128	(200405)	HU		
US 6673794	B2	20040106	(200411)	EN		
NZ 520467	A	20040227	(200418)	EN		
ZA 2002006151	A	20040128	(200420)	EN	135	
EP 1246793	B1	20041110	(200473)	DE		
DE 50008626	G	20041216	(200482)	DE		
AU 780547	B2	20050324	(200528)	EN		
ES 2231312	T3	20050516	(200535)	ES		
MX 226494	B	20050301	(200568)	ES		
HU 225102	B1	20060628	(200649)	HU		
IL 150557	A	20070308	(200726)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10000312 A1		DE 2000-10000312	20000105
BR 2000016942 A		BR 2000-16942	20001227
CN 1437576 A		CN 2000-819265	20001227
DE 50008626 G		DE 2000-508626	20001227
EP 1246793 A2		EP 2000-993710	20001227
EP 1246793 B1		EP 2000-993710	20001227

DE 50008626 G	EP 2000-993710 20001227
ES 2231312 T3	EP 2000-993710 20001227
NZ 520467 A	NZ 2000-520467 20001227
WO 2001049654 A2	WO 2000-EP13281 20001227
EP 1246793 A2	WO 2000-EP13281 20001227
NO 2002002985 A	WO 2000-EP13281 20001227
CZ 2002002337 A3	WO 2000-EP13281 20001227
SK 2002000981 A3	WO 2000-EP13281 20001227
US 20030069288 A1 Cont of	WO 2000-EP13281 20001227
BR 2000016942 A	WO 2000-EP13281 20001227
JP 2003519210 W	WO 2000-EP13281 20001227
MX 2002006700 A1	WO 2000-EP13281 20001227
HU 2002004001 A2	WO 2000-EP13281 20001227
US 6673794 B2 Cont of	WO 2000-EP13281 20001227
NZ 520467 A	WO 2000-EP13281 20001227
EP 1246793 B1	WO 2000-EP13281 20001227
DE 50008626 G	WO 2000-EP13281 20001227
MX 226494 B	WO 2000-EP13281 20001227
HU 225102 B1	WO 2000-EP13281 20001227
AU 2001028438 A	AU 2001-28438 20001227
AU 780547 B2	AU 2001-28438 20001227
JP 2003519210 W	JP 2001-550194 20001227
CZ 2002002337 A3	CZ 2002-2337 20001227
HU 2002004001 A2	HU 2002-4001 20001227
HU 225102 B1	HU 2002-4001 20001227
SK 2002000981 A3	SK 2002-981 20001227
NO 2002002985 A	NO 2002-2985 20020620
KR 2002063294 A	KR 2002-708700 20020704
MX 2002006700 A1	MX 2002-6700 20020705
MX 226494 B	MX 2002-6700 20020705
US 20030069288 A1	US 2002-189190 20020705
US 6673794 B2	US 2002-189190 20020705
ZA 2002006151 A	ZA 2002-6151 20020801
IL 150557 A	IL 2000-150557 20001227

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 780547	B2	Previous Publ	AU 2001028438	A
DE 50008626	G	Based on	EP 1246793	A
ES 2231312	T3	Based on	EP 1246793	A
AU 2001028438	A	Based on	WO 2001049654	A
EP 1246793	A2	Based on	WO 2001049654	A
CZ 2002002337	A3	Based on	WO 2001049654	A
SK 2002000981	A3	Based on	WO 2001049654	A
BR 2000016942	A	Based on	WO 2001049654	A
JP 2003519210	W	Based on	WO 2001049654	A
MX 2002006700	A1	Based on	WO 2001049654	A
HU 2002004001	A2	Based on	WO 2001049654	A
NZ 520467	A	Based on	WO 2001049654	A
EP 1246793	B1	Based on	WO 2001049654	A
DE 50008626	G	Based on	WO 2001049654	A
AU 780547	B2	Based on	WO 2001049654	A
MX 226494	B	Based on	WO 2001049654	A
HU 225102	B1	Based on	WO 2001049654	A
IL 150557	A	Based on	WO 2001049654	A

PRIORITY APPLN. INFO: DE 2000-10000312 20000105
AN 2001-503416 [56] WPIX

AB DE 10000312 A1 UPAB: 20060117
NOVELTY - 4-Alkylidene-1-aminomethyl-2-phenyl-cyclohexane derivatives (I) are new.

DETAILED DESCRIPTION - Cyclohexane derivatives of formula (I), including diastereomers, enantiomers, free bases and acid addition salts, specifically the hydrochloride, are new:

E1, R'1 = H, Q, halo, NR6R'6, NO2, CN, OR6, SR6, OCOR6, COOR6, COR6 or CONR6R'6; or

R1 + R'1 = optionally substituted (os) CH=CH-CH=CH;

Q = alkyl, alkenyl or alkynyl (all os);

R6, R'6 = H, Q, os cycloalkyl (optionally unsaturated and/or having a ring C replaced by N, S or O), os alkylaryl (optionally unsaturated), os aryl or os heteroaryl;

X = H, halo, p-tosyloxy, OR7 or OCOR7; or forms an additional C-C bond with an adjacent ring C to form a cyclohexene ring;

R4, R5, R7 = as R6; or

NR4R5 = os, optionally unsaturated aza-cycloalkyl optionally having a ring C replaced by S, O or NR8;

R8 = H or Q;

R2, R3 = R9 or -Y'-R9;

Y' = Q;

R9 = H, halo, CN or NO2; 1-18C alkyl, 2-18C alkenyl or 2-18C alkynyl (all os); os cycloalkyl (optionally unsaturated and/or having a ring C replaced by NR10, S or O); OR11, OCOR11, OCOOR11, OCSR11, COOR11, CSR11, CSOR11, SR11, SOR11 or SO2R11; or NR13R14, NR13COR14, CONR13R14 or SO2NR13R14;

R10 = H or Q;

R11, R13, R14 = H; 1-18C alkyl, 2-18C alkenyl or 2-18C alkynyl (all os); os cycloalkyl (optionally unsaturated and/or having a ring C replaced by NR12, S or O); or os alkylaryl (optionally unsaturated), os aryl or os heteroaryl;

or R13R14 = os, optionally unsaturated aza-cycloalkyl optionally having a ring C replaced by S, O or NR16; and

R12, R16 = H, Q, os alkylaryl (optionally unsaturated), os aryl or os heteroaryl.

With the proviso that unless specified otherwise alkyl moieties have 1-10C, alkenyl or alkynyl moieties 2-10C and cycloalkyl moieties 3-7C; optionally substituted includes mono- or polysubstitution.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Analgesic; uropathic; antipruritic; antidiarrheic; antiinflammatory; antiallergic; antidepressant; antiaddictive; antialcoholic; cardiant; respiratory; antitussive; anticonvulsant.

In the phenylquinone-induced writhing test for analgesic activity in mice, the hydrochloride of Z-(3-(4-dimethylaminomethyl-3-(3- methoxyphenyl)-cyclohex-2-ylidenemethyl)-phenyl)-methanol (Ia) at 10 mg/kg i.v. gave 100 % inhibition of writhing reaction.

MECHANISM OF ACTION - None given.

USE - (I) are used for treating pain, urinary incontinence, pruritis, diarrhea, inflammatory or allergic reactions, depression, drug and/or alcohol abuse, gastritis, cardiovascular disease, respiratory disease, coughing, mental disease or epilepsy (all claimed). (I) are especially useful as analgesics.

ADVANTAGE - (I) are (almost) free of the side-effects of conventional opioid analgesics (e.g. nausea, emesis, dependency, respiratory depression and constipation).

L28 ANSWER 46 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-290698 [30] WPIX
CROSS REFERENCE: 2001-281963; 2001-281964; 2001-290699; 2001-300210
DOC. NO. CPI: C2001-089106 [30]

TITLE: Nitrogen monoxide synthase inhibitor comprises new or known N-(tert. butyl)-imidazopyridinyl-amine compounds, useful e.g. for treating migraine, septic shock, Parkinson's disease, diabetes or meningitis
DERWENT CLASS: B02
INVENTOR: GERLACH M; HENNIES H; HENNIES H H; MAUL C; SCHNEIDER J; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 90

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001027109	A2	20010419	(200130)*	DE	52[0]	
DE 19948434	A1	20010607	(200132)	DE		
AU 2000079153	A	20010423	(200147)	EN		
EP 1218378	A2	20020703	(200251)	DE		
CZ 2002001241	A3	20020814	(200263)	CS		
SK 2002000462	A3	20020910	(200274)	SK		
US 20030022914	A1	20030130	(200311)	EN		
EP 1218378	B1	20030423	(200329)	DE		
HU 2002003545	A2	20030228	(200330)	HU		
JP 2003511450	W	20030325	(200330)	JA	56	
DE 50001911	G	20030528	(200336)	DE		
CN 1407983	A	20030402	(200345)	ZH		
BR 2000014827	A	20030708	(200364)	PT		
MX 2002003546	A1	20020901	(200370)	ES		
ES 2198355	T3	20040201	(200414)	ES		
US 6703404	B2	20040309	(200418)	EN		
NZ 518438	A	20040827	(200460)	EN		
AU 780526	B2	20050324	(200528)	EN		
MX 225872	B	20050127	(200566)	ES		
IL 148999	A	20070308	(200726)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001027109 A2		WO 2000-EP9791	20001006
DE 19948434 A1		DE 1999-19948434	19991008
AU 2000079153 A		AU 2000-79153	20001006
AU 780526 B2		AU 2000-79153	20001006
BR 2000014827 A		BR 2000-14827	20001006
CN 1407983 A		CN 2000-816707	20001006
DE 50001911 G		DE 2000-501911	20001006
EP 1218378 A2		EP 2000-969439	20001006
EP 1218378 B1		EP 2000-969439	20001006
DE 50001911 G		EP 2000-969439	20001006
ES 2198355 T3		EP 2000-969439	20001006
NZ 518438 A		NZ 2000-518438	20001006
EP 1218378 A2		WO 2000-EP9791	20001006
CZ 2002001241 A3		WO 2000-EP9791	20001006
SK 2002000462 A3		WO 2000-EP9791	20001006
US 20030022914 A1	Cont of	WO 2000-EP9791	20001006
EP 1218378 B1		WO 2000-EP9791	20001006
JP 2003511450 W		WO 2000-EP9791	20001006
HU 2002003545 A2		WO 2000-EP9791	20001006
DE 50001911 G		WO 2000-EP9791	20001006
BR 2000014827 A		WO 2000-EP9791	20001006

MX 2002003546 A1	WO 2000-EP9791 20001006
US 6703404 B2 Cont of	WO 2000-EP9791 20001006
NZ 518438 A	WO 2000-EP9791 20001006
MX 225872 B	WO 2000-EP9791 20001006
JP 2003511450 W	JP 2001-530327 20001006
CZ 2002001241 A3	CZ 2002-1241 20001006
HU 2002003545 A2	HU 2002-3545 20001006
SK 2002000462 A3	SK 2002-462 20001006
MX 2002003546 A1	MX 2002-3546 20020408
MX 225872 B	MX 2002-3546 20020408
US 20030022914 A1	US 2002-117339 20020408
US 6703404 B2	US 2002-117339 20020408
IL 148999 A	IL 2000-148999 20001006

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 780526	B2	Previous Publ	AU 2000079153	A
DE 50001911	G	Based on	EP 1218378	A
ES 2198355	T3	Based on	EP 1218378	A
AU 2000079153	A	Based on	WO 2001027109	A
EP 1218378	A2	Based on	WO 2001027109	A
CZ 2002001241	A3	Based on	WO 2001027109	A
SK 2002000462	A3	Based on	WO 2001027109	A
EP 1218378	B1	Based on	WO 2001027109	A
JP 2003511450	W	Based on	WO 2001027109	A
HU 2002003545	A2	Based on	WO 2001027109	A
DE 50001911	G	Based on	WO 2001027109	A
BR 2000014827	A	Based on	WO 2001027109	A
MX 2002003546	A1	Based on	WO 2001027109	A
NZ 518438	A	Based on	WO 2001027109	A
AU 780526	B2	Based on	WO 2001027109	A
MX 225872	B	Based on	WO 2001027109	A
IL 148999	A	Based on	WO 2001027109	A

PRIORITY APPLN. INFO: DE 1999-19948434 19991008
AN 2001-290698 [30] WPIX
CR 2001-281963; 2001-281964; 2001-290699; 2001-300210
AB WO 2001027109 A2 UPAB: 20060117

NOVELTY - Nitrogen monoxide synthase inhibitor comprises tert. butyl-(7-methyl-imidazo(1,2-a)pyridin-3-yl)-amine derivatives (I). Most of (I) are new compounds.

DETAILED DESCRIPTION - Nitrogen monoxide synthase inhibitor comprises tert. butyl-(7-methyl-imidazo(1,2-a)pyridin-3-yl)-amine derivatives (I) or their salts.

R1 = H or optionally mono- or poly-substituted 1-4C alkyl;

R2 = alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, alkyl-cycloalkyl, alkyl-heterocyclyl, alkyl-aryl or alkyl-heteroaryl (where alkyl, cycloalkyl and heterocyclyl are optionally unsaturated and alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally mono- or poly-substituted);

unless specified otherwise alkyl groups have 1-8C and cycloalkyl groups 3-8C.

INDEPENDENT CLAIMS are included for the following:

(i) new (I) and their salts, with the exception of (I; R1 = Me; R2 = Ph) and

(ii) preparation of new compounds (I).

ACTIVITY - Antibacterial; immunosuppressive; neuroprotective; antiparkinsonian; nootropic; antiinflammatory; analgesic; cerebroprotective; vasotropic; antidiabetic; antiarteriosclerotic; vulnerary.

MECHANISM OF ACTION - Nitrogen monoxide synthase (NOS) inhibitor.

In a high throughput screening assay, tert. butyl-(2-cyclohexyl- 5,7-dimethyl-imidazo (1,2-a) pyridin-3-yl)-amine (Ia) at 10 micro-M gave 68% inhibition of NOS, compared with 50% for the known inhibitor 7-nitroindazole.

USE - Useful for treating migraine, septic shock, multiple sclerosis, Parkinson's disease, Alzheimer's disease, Huntington's disease, inflammation, inflammatory pain, cerebral ischemia, diabetes, meningitis, arteriosclerosis and/or wound healing deficiency (all claimed).

L28 ANSWER 47 OF 47 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-603904 [58] WPIX
DOC. NO. CPI: C2000-180812 [58]
TITLE: New 3-amino-3-aryl-propan-1-ol and 3-amino-3-heteroaryl-propan-1-ol benzyl ether and benzoate ester derivatives useful as analgesics, local anaesthetics, antiarrhythmics, antiemetics and nootropics
DERWENT CLASS: B05
INVENTOR: BUSCHMANN H; COGER B -; HENNIES H; HENNIES H H; HENNIS H -; KOEGEL B; KOEGEL B Y; KOGEL B; SUDERMANN B; SUNDERMANN B
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 40

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 1043306	A2	20001011	(200058)*	DE	17[0]	
AU 2000026450	A	20001012	(200058)	EN		
NO 2000001782	A	20001009	(200058)	NO		
SK 2000000495	A3	20001009	(200058)	SK		
CA 2303721	A1	20001007	(200059)	EN		
DE 19915602	A1	20001019	(200060)	DE		
CZ 2000001251	A3	20001115	(200064)	CS		
JP 2000327643	A	20001128	(200065)	JA	13	
CN 1270163	A	20001018	(200103)	ZH		
ZA 2000001747	A	20001227	(200103)	EN	42	
NZ 503397	A	20010427	(200128)	EN		
KR 2000071570	A	20001125	(200131)	KO		
US 6288278	B1	20010911	(200154)	EN		
BR 2000008681	A	20020226	(200223)	PT		
HU 2000001397	A1	20020429	(200238)	HU		
MX 2000003286	A1	20020301	(200362)	ES		
IL 135452	A	20040208	(200415)	EN		
EP 1043306	B1	20040331	(200426)	DE		
DE 50005841	G	20040506	(200434)	DE		
ES 2218016	T3	20041116	(200477)	ES		
AU 777873	B2	20041104	(200504)	EN		
MX 225337	B	20050104	(200566)	ES		
CN 1147461	C	20040428	(200610)	ZH		
US 39530	E	20070327	(200724)	EN		
NO 325029	B1	20080121	(200815)	NO		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1043306 A2		EP 2000-104740	20000304
DE 19915602 A1		DE 1999-19915602	19990407

DE 50005841 G	DE 2000-50005841 20000304
DE 50005841 G	EP 2000-104740 20000304
ES 2218016 T3	EP 2000-104740 20000304
NZ 503397 A	NZ 2000-503397 20000314
IL 135452 A	IL 2000-135452 20000404
MX 2000003286 A1	MX 2000-3286 20000404
MX 225337 B	MX 2000-3286 20000404
BR 2000008681 A	BR 2000-8681 20000405
CA 2303721 A1	CA 2000-2303721 20000405
HU 2000001397 A1	HU 2000-1397 20000405
AU 2000026450 A	AU 2000-26450 20000406
AU 777873 B2	AU 2000-26450 20000406
CN 1270163 A	CN 2000-104980 20000406
CN 1147461 C	CN 2000-104980 20000406
CZ 2000001251 A3	CZ 2000-1251 20000406
JP 2000327643 A	JP 2000-105260 20000406
KR 2000071570 A	KR 2000-17864 20000406
NO 2000001782 A	NO 2000-1782 20000406
SK 2000000495 A3	SK 2000-495 20000406
ZA 2000001747 A	ZA 2000-1747 20000406
US 6288278 B1	US 2000-545519 20000407
US 39530 E	US 2000-545519 20000407
US 39530 E	US 2003-659680 20030911
NO 325029 B1	NO 2000-1782 20000406

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 777873	B2	Previous Publ	AU 2000026450	A
DE 50005841	G	Based on	EP 1043306	A
ES 2218016	T3	Based on	EP 1043306	A
US 39530	E	Reissue of	US 6288278	B
NO 325029	B1	Previous Publ	NO 2000001782	A

PRIORITY APPLN. INFO: DE 1999-19915602 19990407
AN 2000-603904 [58] WPIX
AB EP 1043306 A2 UPAB: 20060822
NOVELTY - 3-Amino-3-(hetero)aryl-propan-1-ol benzyl ethers and benzoate esters (I) are new.

DETAILED DESCRIPTION - The 3-amino-3-(hetero)aryl-propan-1-ol benzyl ether and benzyl esters are compounds of formula (I), including their enantiomers and diastereoisomers, and their addition salts.

A = aryl optionally containing hetero atoms;

R1, R2 = 1-6C alkyl; or

R1 + R2 = form 2-6C alkylidene optionally benzo-fused or substituted with phenyl;

R3 = H or CH3;

R4, R5 = 1-6C alkyl, 3-6C cycloalkyl, phenyl, benzyl or phenethyl; or

R4 + R5 = form 3-6C alkylidene or -CH2CH2OCH2CH2- ;

X = group of formula (i) or (ii);

R12-R14 = H, F, Cl, Br, CHF2, CF3, OR11, SR11, OCF3, SO2CH3, SO2CF3, 1-6C alkyl, phenyl, CN, COOR11 or NO2; and

R11 = H, 1-6C alkyl, phenyl, benzyl or phenethyl.

An INDEPENDENT CLAIM is also included for the preparation of compounds (I).

ACTIVITY - Analgesic; local anaesthetic; antiarrhythmic; antiemetic; nootropic; antiinflammatory; cardiant; uropathic; antidiarrheic; antialcoholic; antiaddictive. In the writhing test carried out on mice dimethyl-((2-(2-methylbenzyloxy)cyclohexyl)phenylmethyl)ami ne gave 85 % inhibition of the

writhing reaction when administered i.v.
at 10 mg/kg.
MECHANISM OF ACTION - Sodium channel blocker (binding to binding site 2 of the sodium channel (BTX binding)); L-potassium channel blocker (binding to the benzothiazepine binding site of the L-type potassium channel (diltiazem binding)). ((2-(3-Fluorobenzyloxy)cyclohexyl)phenylmethyl)dimethylamine HCl (I) gave 89 % inhibition of diltiazem binding and 98 % inhibition of BTX binding when used in a concentration of 10 microM.
USE - Compounds (I) are useful for the control of pain, especially neuropathic and chronic pain, and as local anaesthetics, antiarrythmics, antiemetics and nootropics. They are also useful for the treatment of cardiovascular disorders, urinary incontinence, diarrhea, pruritis, inflammation and dependence on alcohol, drugs or other medicaments.
ADVANTAGE - Compounds (I) have pronounced analgesic activity and are toxicologically harmless.

Member(0006)
ABEQ DE 19915602 A1 UPAB 20060822
NOVELTY - 3-Amino-3-(hetero)aryl-propan-1-ol benzyl ethers and benzoate esters (I) are new.
DETAILED DESCRIPTION - The 3-amino-3-(hetero)aryl-propan-1-ol benzyl ether and benzyl esters are compounds of formula (I), including their enantiomers and diastereoisomers, and their addition salts.
A = aryl optionally containing hetero atoms;
R1, R2 = 1-6C alkyl; or
R1 + R2 = form 2-6C alkylidene optionally benzo-fused or substituted with phenyl;
R3 = H or CH3;
R4, R5 = 1-6C alkyl, 3-6C cycloalkyl, phenyl, benzyl or phenethyl; or
R4 + R5 = form 3-6C alkylidene or -CH2CH2OCH2CH2- ;
X = group of formula (i) or (ii);
R12-R14 = H, F, Cl, Br, CHF2, CF3, OR11, SR11, OCF3, SO2CH3, SO2CF3, 1-6C alkyl, phenyl, CN, COOR11 or NO2; and
R11 = H, 1-6C alkyl, phenyl, benzyl or phenethyl.
An INDEPENDENT CLAIM is also included for the preparation of compounds (I).
ACTIVITY - Analgesic; local anaesthetic; antiarrhythmic; antiemetic; nootropic; antiinflammatory; cardiant; uropathic; antidiarrheic; antialcoholic; antiaddictive. In the writhing test carried out on mice dimethyl-((2-(2-methylbenzyloxy)cyclohexyl)phenylmethyl)amine gave 85 % inhibition of the writhing reaction when administered i.v. at 10 mg/kg.
MECHANISM OF ACTION - Sodium channel blocker (binding to binding site 2 of the sodium channel (BTX binding)); L-potassium channel blocker (binding to the benzothiazepine binding site of the L-type potassium channel (diltiazem binding)). ((2-(3-Fluorobenzyloxy)cyclohexyl)phenylmethyl)dimethylamine HCl (I) gave 89 % inhibition of diltiazem binding and 98 % inhibition of BTX binding when used in a concentration of 10 microM.
USE - Compounds (I) are useful for the control of pain, especially neuropathic and chronic pain, and as local anaesthetics, antiarrythmics, antiemetics and nootropics. They are also useful for the treatment of cardiovascular disorders, urinary incontinence, diarrhea, pruritis, inflammation and dependence on alcohol, drugs or other medicaments.
ADVANTAGE - Compounds (I) have pronounced analgesic activity and are toxicologically harmless.

Member(0008)
ABEQ JP 2000327643 A UPAB 20060822
NOVELTY - 3-Amino-3-(hetero)aryl-propan-1-ol benzyl ethers and benzoate

esters (I) are new.
DETAILED DESCRIPTION - The 3-amino-3-(hetero)aryl-propan-1-ol benzyl ether and benzyl esters are compounds of formula (I), including their enantiomers and diastereoisomers, and their addition salts.
A = aryl optionally containing hetero atoms;
R1, R2 = 1-6C alkyl; or
R1 + R2 = form 2-6C alkylidene optionally benzo-fused or substituted with phenyl;
R3 = H or CH3;
R4, R5 = 1-6C alkyl, 3-6C cycloalkyl, phenyl, benzyl or phenethyl; or
R4 + R5 = form 3-6C alkylidene or -CH2CH2OCH2CH2- ;
X = group of formula (i) or (ii);
R12-R14 = H, F, Cl, Br, CHF2, CF3, OR11, SR11, OCF3, SO2CH3, SO2CF3, 1-6C alkyl, phenyl, CN, COOR11 or NO2; and
R11 = H, 1-6C alkyl, phenyl, benzyl or phenethyl.
An INDEPENDENT CLAIM is also included for the preparation of compounds (I).
ACTIVITY - Analgesic; local anaesthetic; antiarrhythmic; antiemetic; nootropic; antiinflammatory; cardiant; uropathic; antidiarrheic; antialcoholic; antiaddictive. In the writhing test carried out on mice dimethyl-((2-(2-methylbenzyloxy)cyclohexyl)phenylmethyl)amine gave 85 % inhibition of the writhing reaction when administered i.v. at 10 mg/kg.
MECHANISM OF ACTION - Sodium channel blocker (binding to binding site 2 of the sodium channel (BTX binding)); L-potassium channel blocker (binding to the benzothiazepine binding site of the L-type potassium channel (diltiazem binding)). ((2-(3-Fluorobenzyloxy)cyclohexyl)phenylmethyl)dimethylamine HCl (I) gave 89 % inhibition of diltiazem binding and 98 % inhibition of BTX binding when used in a concentration of 10 microM.
USE - Compounds (I) are useful for the control of pain, especially neuropathic and chronic pain, and as local anaesthetics, antiarrythmics, antiemetics and nootropics. They are also useful for the treatment of cardiovascular disorders, urinary incontinence, diarrhea, pruritis, inflammation and dependence on alcohol, drugs or other medicaments.
ADVANTAGE - Compounds (I) have pronounced analgesic activity and are toxicologically harmless.

Member(0009)
ABEQ CN 1270163 A UPAB 20060822
NOVELTY - 3-Amino-3-(hetero)aryl-propan-1-ol benzyl ethers and benzoate esters (I) are new.
DETAILED DESCRIPTION - The 3-amino-3-(hetero)aryl-propan-1-ol benzyl ether and benzyl esters are compounds of formula (I), including their enantiomers and diastereoisomers, and their addition salts.
A = aryl optionally containing hetero atoms;
R1, R2 = 1-6C alkyl; or
R1 + R2 = form 2-6C alkylidene optionally benzo-fused or substituted with phenyl;
R3 = H or CH3;
R4, R5 = 1-6C alkyl, 3-6C cycloalkyl, phenyl, benzyl or phenethyl; or
R4 + R5 = form 3-6C alkylidene or -CH2CH2OCH2CH2- ;
X = group of formula (i) or (ii);
R12-R14 = H, F, Cl, Br, CHF2, CF3, OR11, SR11, OCF3, SO2CH3, SO2CF3, 1-6C alkyl, phenyl, CN, COOR11 or NO2; and
R11 = H, 1-6C alkyl, phenyl, benzyl or phenethyl.
An INDEPENDENT CLAIM is also included for the preparation of compounds (I).
ACTIVITY - Analgesic; local anaesthetic; antiarrhythmic;

antiemetic; nootropic; antiinflammatory; cardiant; uropathic; antidiarrheic; antialcoholic; antiaddictive. In the writhing test carried out on mice dimethyl-((2-(2-methylbenzyloxy)cyclohexyl)phenylmethyl)amine gave 85 % inhibition of the writhing reaction when administered i.v. at 10 mg/kg.

MECHANISM OF ACTION - Sodium channel blocker (binding to binding site 2 of the sodium channel (BTX binding)); L-potassium channel blocker (binding to the benzothiazepine binding site of the L-type potassium channel (diltiazem binding)). ((2-(3-Fluorobenzyloxy)cyclohexyl)phenylmethyl)dimethylamine HCl (I) gave 89 % inhibition of diltiazem binding and 98 % inhibition of BTX binding when used in a concentration of 10 microM.

USE - Compounds (I) are useful for the control of pain, especially neuropathic and chronic pain, and as local anaesthetics, antiarrythmics, antiemetics and nootropics. They are also useful for the treatment of cardiovascular disorders, urinary incontinence, diarrhea, pruritis, inflammation and dependence on alcohol, drugs or other medicaments.

ADVANTAGE - Compounds (I) have pronounced analgesic activity and are toxicologically harmless.

Member(0010)

ABEQ ZA 200001747 A UPAB 20060822

NOVELTY - 3-Amino-3-(hetero)aryl-propan-1-ol benzyl ethers and benzoate esters (I) are new.

DETAILED DESCRIPTION - The 3-amino-3-(hetero)aryl-propan-1-ol benzyl ether and benzyl esters are compounds of formula (I), including their enantiomers and diastereoisomers, and their addition salts.

A = aryl optionally containing hetero atoms;

R1, R2 = 1-6C alkyl; or

R1 + R2 = form 2-6C alkylidene optionally benzo-fused or substituted with phenyl;

R3 = H or CH3;

R4, R5 = 1-6C alkyl, 3-6C cycloalkyl, phenyl, benzyl or phenethyl; or

R4 + R5 = form 3-6C alkylidene or -CH2CH2OCH2CH2- ;

X = group of formula (i) or (ii);

R12-R14 = H, F, Cl, Br, CHF2, CF3, OR11, SR11, OCF3, SO2CH3, SO2CF3, 1-6C alkyl, phenyl, CN, COOR11 or NO2; and

R11 = H, 1-6C alkyl, phenyl, benzyl or phenethyl.

An INDEPENDENT CLAIM is also included for the preparation of compounds (I).

ACTIVITY - Analgesic; local anaesthetic; antiarrhythmic; antiemetic; nootropic; antiinflammatory; cardiant; uropathic; antidiarrheic; antialcoholic; antiaddictive. In the writhing test carried out on mice dimethyl-((2-(2-methylbenzyloxy)cyclohexyl)phenylmethyl)amine gave 85 % inhibition of the writhing reaction when administered i.v. at 10 mg/kg.

MECHANISM OF ACTION - Sodium channel blocker (binding to binding site 2 of the sodium channel (BTX binding)); L-potassium channel blocker (binding to the benzothiazepine binding site of the L-type potassium channel (diltiazem binding)). ((2-(3-Fluorobenzyloxy)cyclohexyl)phenylmethyl)dimethylamine HCl (I) gave 89 % inhibition of diltiazem binding and 98 % inhibition of BTX binding when used in a concentration of 10 microM.

USE - Compounds (I) are useful for the control of pain, especially neuropathic and chronic pain, and as local anaesthetics, antiarrythmics, antiemetics and nootropics. They are also useful for the treatment of cardiovascular disorders, urinary incontinence, diarrhea, pruritis, inflammation and dependence on alcohol, drugs or other medicaments.

ADVANTAGE - Compounds (I) have pronounced analgesic activity and are toxicologically harmless.

Member(0013)
ABEQ US 6288278 B1 UPAB 20060822
NOVELTY - 3-Amino-3-(hetero)aryl-propan-1-ol benzyl ethers and benzoate esters (I) are new.
DETAILED DESCRIPTION - The 3-amino-3-(hetero)aryl-propan-1-ol benzyl ether and benzyl esters are compounds of formula (I), including their enantiomers and diastereoisomers, and their addition salts.
A = aryl optionally containing hetero atoms;
R1, R2 = 1-6C alkyl; or
R1 + R2 = form 2-6C alkylidene optionally benzo-fused or substituted with phenyl;
R3 = H or CH3;
R4, R5 = 1-6C alkyl, 3-6C cycloalkyl, phenyl, benzyl or phenethyl; or
R4 + R5 = form 3-6C alkylidene or -CH2CH2OCH2CH2- ;
X = group of formula (i) or (ii);
R12-R14 = H, F, Cl, Br, CHF2, CF3, OR11, SR11, OCF3, SO2CH3, SO2CF3, 1-6C alkyl, phenyl, CN, COOR11 or NO2; and
R11 = H, 1-6C alkyl, phenyl, benzyl or phenethyl.
An INDEPENDENT CLAIM is also included for the preparation of compounds (I).
ACTIVITY - Analgesic; local anaesthetic; antiarrhythmic; antiemetic; nootropic; antiinflammatory; cardiant; uropathic; antidiarrheic; antialcoholic; antiaddictive. In the writhing test carried out on mice dimethyl-((2-(2-methylbenzyloxy)cyclohexyl)phenylmethyl)amine gave 85 % inhibition of the writhing reaction when administered i.v. at 10 mg/kg.
MECHANISM OF ACTION - Sodium channel blocker (binding to binding site 2 of the sodium channel (BTX binding)); L-potassium channel blocker (binding to the benzothiazepine binding site of the L-type potassium channel (diltiazem binding)). ((2-(3-Fluorobenzyloxy)cyclohexyl)phenylmethyl)dimethylamine HCl (I) gave 89 % inhibition of diltiazem binding and 98 % inhibition of BTX binding when used in a concentration of 10 microM.
USE - Compounds (I) are useful for the control of pain, especially neuropathic and chronic pain, and as local anaesthetics, antiarrythmics, antiemetics and nootropics. They are also useful for the treatment of cardiovascular disorders, urinary incontinence, diarrhea, pruritis, inflammation and dependence on alcohol, drugs or other medicaments.
ADVANTAGE - Compounds (I) have pronounced analgesic activity and are toxicologically harmless.

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(FILE 'HOME' ENTERED AT 11:53:40 ON 28 MAR 2008)

FILE 'REGISTRY' ENTERED AT 11:53:45 ON 28 MAR 2008
L1 STR
L2 STR L1
L3 3 SEA SSS SAM L2
L4 190 SEA SSS FUL L2

FILE 'CAPLUS' ENTERED AT 11:59:01 ON 28 MAR 2008
L5 19 SEA ABB=ON PLU=ON L4
E US2004-758241/APPS
L6 1 SEA ABB=ON PLU=ON US2004-758241/AP
SEL RN

FILE 'REGISTRY' ENTERED AT 11:59:47 ON 28 MAR 2008
L7 69 SEA ABB=ON PLU=ON (123-75-1/BI OR 151-67-7/BI OR 25017-13-4/B

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                I OR 271-89-6/BI OR 2932-58-3/BI OR 332-42-3/BI OR 345-35-7/BI
                OR 352-11-4/BI OR 451-82-1/BI OR 456-42-8/BI OR 4746-97-8/BI
                OR 475098-33-0/BI OR 475098-34-1/BI OR 492461-57-1/BI OR
                492461-58-2/BI OR 492461-59-3/BI OR 492461-60-6/BI OR 492461-61
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                492461-81-1/BI OR 492461-83-3/BI OR 492461-85-5/BI OR 492461-88
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                492462-27-8/BI OR 56-29-1/BI OR 57-27-2/BI OR 603-76-9/BI OR
                627-37-2/BI OR 65619-92-3/BI OR 65620-18-0/BI OR 6921-34-2/BI
                OR 7342-82-7/BI OR 75489-29-1/BI OR 90878-19-6/BI OR 91319-54-9
                /BI OR 95-15-8/BI)
L8           32 SEA ABB=ON  PLU=ON  L7 AND L4
L9           37 SEA ABB=ON  PLU=ON  L7 NOT L8
L10          25 SEA ABB=ON  PLU=ON  L9 AND C6/ES
                D SCA

     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:02:46 ON 28 MAR 2008
                E SUNDERMANN B/AU
L11         176 SEA ABB=ON  PLU=ON  ("SUNDERMANN B"/AU OR "SUNDERMANN BERND"/AU
                 OR "SUNDERMANN BERNHARD"/AU OR "SUNDERMANN BERNHARDT"/AU)
                E HENNIES H/AU
L12         136 SEA ABB=ON  PLU=ON  ("HENNIES H"/AU OR "HENNIES H "/AU OR
                "HENNIES H H"/AU OR "HENNIES HAGEN H"/AU OR "HENNIES HAGEN
                HEINRICH"/AU)
                E HEINRICH HENN/AU
                E KOEGEL B/AU
L13          83 SEA ABB=ON  PLU=ON  ("KOEGEL B"/AU OR "KOEGEL B "/AU OR
                "KOEGEL B Y"/AU OR "KOEGEL BABETTE"/AU OR "KOEGEL BABETTE
                YVONNE"/AU)
                E WNENDT S/AU
L14          68 SEA ABB=ON  PLU=ON  ("WNENDT S"/AU OR "WNENDT STEPHAN"/AU)
L15         354 SEA ABB=ON  PLU=ON  (L11 OR L12 OR L13 OR L14)
L16         125 SEA ABB=ON  PLU=ON  L15 AND (?CYCLOHEX? OR AMINOCYCLOHEX?)
L17          77 SEA ABB=ON  PLU=ON  L16 AND AMINO?
L18          59 SEA ABB=ON  PLU=ON  L15 AND (AMIN?(S) CYCLOHEX? OR AMINOCYCLOHE
                X?)

     FILE 'CAPLUS' ENTERED AT 12:06:56 ON 28 MAR 2008
                D QUE L5
                D L5 IBIB ABS HITSTR TOT
L19           3 SEA ABB=ON  PLU=ON  L5 AND (SUNDERMANN?/AU OR HENNIES?/AU OR
                KOEGEL B?/AU OR WNENDT?/AU)

     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:08:45 ON 28 MAR 2008
                D QUE L18
L20          50 DUP REM L18 (9 DUPLICATES REMOVED)
                      ANSWERS '1-22' FROM FILE CAPLUS
                      ANSWERS '23-50' FROM FILE WPIX
                D SCA TI L19
L21          49 SEA ABB=ON  PLU=ON  L20 NOT PREPARATION OF CYCLOHEXYLINDOLES
                AS OPIOID RECEPTOR?/TI
L22          47 SEA ABB=ON  PLU=ON  L21 NOT PREPARATION OF SUBSTITUTED
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      4-AMINOCYCLOHEXANOLS?/TI
L23       49 SEA ABB=ON  PLU=ON  L21 NOT "PREPARATION OF SUBSTITUTED
      4-AMINOCYCLOHEXANOLS AS REGULATORS FOR THE NOCICEPTIN/ORPHANIN
      FQ LIGAND ORL-1 RECEPTOR SYSTEM"/TI
L24       49 SEA ABB=ON  PLU=ON  L21 NOT "PREPARATION OF SUBSTITUTED
      4-AMINOCYCLOHEXANOLS AS REGULATORS FOR THE"/TI
L25       49 SEA ABB=ON  PLU=ON  L24 NOT "PREPARATION OF 4-AMINO-4-(ARYLALKY
      L)CYCLOHEXANOLS AS ORL1 RECEPTOR LIGANDS"/TI
L26       48 SEA ABB=ON  PLU=ON  L21 NOT PREPARATION OF SUBSTITUTED
      4-AMINOCYCLOHEXANOLS AS REGULATORS FOR THE NOCICEPTIN?/TI
L27       48 SEA ABB=ON  PLU=ON  L26 NOT "PREPARATION OF 4-AMINO-4-(ARYLALKY
      L)CYCLOHEXANOLS AS ORL1 RECEPTOR LIGANDS FOR TREATMENT OF
      PAIN"/TI
L28       47 SEA ABB=ON  PLU=ON  L26 NOT AS ORL1 RECEPTOR LIGANDS?/TI
      D  L28 IBIB ABS TOT
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